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ABSTRACTS OF WORLD MEDICINE

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ABSTRACTS OF WORLD MEDICINE

UNDER THE DIRECTION OF

HUGH CLEGG, M.A., M.B., F.R.C.P., Editor, *BRITISH MEDICAL JOURNAL*

EDITED BY

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This journal is planned to provide the reader with a selection of abstracts of the more important articles appearing in medical periodicals published in different parts of the world. Comment by the abstracter, when thought necessary, is inserted between square brackets, usually at the end of an abstract. In some instances only the titles of articles are provided.

After the title of each journal from which an abstract is taken we print the abbreviation given in the *World List of Scientific Periodicals*. The titles of articles from foreign journals are translated into English.

This journal is essentially a guide to work in progress in the world's medical centres. No abstract can be regarded as a substitute for the article abstracted. For complete information the original article must be consulted. Our aim is to give the reader sufficient details in an abstract to enable him to judge whether the original is, for him, worth reading in full.

The abstracts are grouped in broad classifications which represent the special fields of study into which Medicine is divided. The specialist will, it is hoped, learn from this journal of work done in other fields as well as in his own. The general practitioner will be able to keep abreast of modern knowledge in the various specialties. The representation in one journal of the several aspects of Medicine will, it is believed, give an integrated picture of the whole, necessary in this age of specialization.

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ABSTRACTS OF WORLD MEDICINE

VOL. 11 NOS. 5–6 MAY–JUNE, 1952

STATEMENT TO SUBSCRIBERS

FROM THE EDITOR, *BRITISH MEDICAL JOURNAL*

With the sudden death of the Editor of this journal, Dr. G. M. Findlay, on March 14, 1952, the medical profession lost a man who in the laboratory, the library, and the editorial chair had given for many years, and indefatigably, of his best. Dr. Findlay had edited *Abstracts of World Medicine* from its inception in January, 1947, and his sudden and grievous loss has confronted us with problems not easily to be solved. In attempting to grapple with immediate difficulties we must crave the forbearance of subscribers.

During the past eighteen months those responsible for the publications of the British Medical Association have been faced with a steep rise in the costs of production, brought about principally by the rapid rise in the price of paper, which in itself drove out of circulation fifty-one periodicals in 1951. The cost of the Abstracting Service to the B.M.A. is heavy, and in the weeks before Dr. Findlay's death ways and means of reducing this were being closely examined.

The Council of the B.M.A. had already decided that for financial reasons alone *Abstracts of World Surgery, Obstetrics and Gynaecology* should be discontinued after June, 1952. Much of what appears in that journal will be merged into a remodelled *Abstracts of World Medicine*. If all goes well, the first number of this remodelled journal will appear in July, 1952, and it is hoped that its appeal to the clinical worker will be enhanced.

We would apologize to subscribers for the recent delay in publication. This is the result of a number of factors, not least among them being a succession of changes in staff that has thrown an exceptionally heavy burden on those who have carried on the work. Dr. Findlay's death came as a crowning misfortune.

In order to relieve the pressure of work and to catch up arrears four issues only instead of six are being published in the first half of 1952. The third and fourth issues for this year were published as one, as are the fifth and sixth issues. From July onwards the remodelled *Abstracts of World Medicine* will appear regularly each month, and in a form which we hope will progressively appeal to the clinical worker in hospital and consulting practice.

The circumstances that have compelled these decisions are unprecedented, but the support given by subscribers to the abstracting service since 1947 encourages us to go ahead with plans for making *Abstracts of World Medicine* a trustworthy guide through the maze of modern medicine.

HUGH CLEGG

Morphology and Genetics

1112. **Arteries, Veins, and Arteriovenous Anastomosis in the Human Stomach**
T. E. BARLOW, F. H. BENTLEY, and D. N. WALDER. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **93**, 657–671, Dec., 1951. 30 figs., 12 refs.

The authors have studied the general pattern of vessels supplying the normal human stomach in specimens removed post mortem, while for more detailed survey they used specimens consisting of the distal two-thirds of the stomach removed at operation for duodenal ulcer from young and middle-aged males. For microradiography the contrast medium was injected through the gastro-epiploic artery and/or vein under a pressure of 130 mm. of mercury at 37° C.; 20% bismuth oxychloride was used to define the arteries and arterioles, preceded by 10% colloidal silver iodide if it was desired to show the capillaries as well. After injection the specimen was fixed in 10% formol saline for 48 hours, being opened along the greater curvature after the first 24 hours. After radiography of the whole stomach, transverse frozen sections 400 μ thick were radiographed at 20 kV and 20 mA by means of a soft *x*-ray tube with a molybdenum target and a thin beryllium window.

Microdissection of the stomach was carried out after injection of 10% gelatin in saline or human plasma with the addition of 5% colouring agent. In some experiments capillary filling was prevented by adding 20% rice-starch granules 20 μ in diameter. To fill all the vessels red gelatin was injected into the artery at a pressure of 130 mm. mercury, followed by an injection of blue gelatin containing rice starch into the vein at a pressure of 80 mm. mercury. To exclude the capillaries the vessels were washed out with isotonic saline and both the artery and vein were injected simultaneously, each injection containing rice starch. After fixation in 10% formol saline the specimens were opened up and the muscle coat removed. They were then cleared by immersion for 7 days each in the following solutions: 2% sodium hydroxide; 20%, 40%, 60%, and 80% glycerin; and finally in pure glycerin.

The anterior and posterior walls of the stomach were found to be supplied by branches which arise from the main arteries at intervals of about 1 cm. and, after piercing the muscle coats, form an extensive submucous plexus. These vessels are about 200 μ in diameter, and the loops of the plexus are further cross-connected by vessels of about 150 μ in diameter. The plexus in the pyloric region is, however, of smaller extent, and the vessels are only 100 to 150 μ wide. From the submucous plexus arise the mucosal arteries, which are interconnected by channels 150 μ wide just outside the muscularis mucosae. The mucosal artery then breaks up into 3 or 4 branches which, after a tortuous course, pierce the muscularis and form another anastomosing network, from which arise the vessels of the mucous membrane. These consist of vertically-running capillaries of 20 μ diameter giving off smaller capillaries (8 μ) which ramify among the glands.

In the region of the lesser curve the mucosal arteries arise direct from the gastric arteries, the submucous plexus being absent. These arteries are only 60 to 100 μ in diameter. The rest of their course is similar to that of the vessels in other regions of the stomach, and the same number of branches piercing the muscularis mucosae is present in all regions (90 to 120 branches per sq. cm.).

In the submucosa are found arterio-venous anastomoses of the direct (non-glomus) type, usually joining a mucosal artery to a mucosal vein or the submucous venous plexus. In the narrowest part of the anastomosis the lumen may be almost occluded in the fixed specimen, and in this region cells of the musculo-epithelial type could be identified. The submucosa also possesses an entirely self-contained plexus of arteries and veins, the latter frequently showing multiple local dilatations.

The arterio-venous anastomoses were further investigated in excised stomachs by the glass-sphere method, and it was found that they have a maximum size of 140 μ. Conditions which increase the rate of flow through the stomach vessels are associated with a decreased flow through the anastomoses, and vice versa

D. B. Moffat

1113. **The Anatomy and Applied Anatomy of the Mediastinal Fascia**
P. MARCHAND. *Thorax* [*Thorax*] **6**, 359–368, Dec., 1951. 14 figs., 19 refs.

The mediastinal fasciae were investigated in 12 heart-and-lung specimens from adults who had died of extra-thoracic causes, a radio-opaque coloured fluid being injected into the space between the trachea and the pretracheal fascia or into the perihilar tissues, and subsequent radiography and dissection performed.

The pretracheal fascia forms a complete investing layer to trachea and oesophagus; this perivisceral fascia is prolonged into the mediastinum, where its anterior aspect becomes continuous with the fibrous layer of the parietal pericardium. The latter is loosely separated from the serous layer around the origin of the aorta, and it supplies fascial sheaths which invest all the great vessels except the inferior vena cava. The perivisceral fascia is continued as an investing layer over the bronchi, following them to their third or fourth division, where it appears to become adherent. The bronchial vessels, lymphatics, and lymph nodes lie within this fascia.

When the pleurae are fused, stab wounds of the lung may cause mediastinal emphysema, the air tracking in this peribronchial plane. This may also occur with the spontaneous rupture of a bronchus or of an emphysematous bulla, as occasionally happens during labour. The

" bat's-wing " shadow sometimes seen in the chest radiograph of patients with hypertensive heart failure corresponds with the anatomical extent of the perivascular and peribronchial spaces, and is probably due to oedema in them. The relationship of the pericardium to the perivisceral spaces, in which lie lymph nodes, explains why caseating mediastinal nodes are often associated with tuberculous pericarditis. *M. Meredith Brown*

1114. **Observations on the Normal Anatomy of the Bronchial Arteries**
L. CUDKOWICZ and J. B. ARMSTRONG. *Thorax* [*Thorax*] **6**, 343–358, Dec., 1951. 14 figs., 20 refs.

1115. **Morphological Patterns in Limb Deficiencies and Duplications**
R. O'RAHILLY. *American Journal of Anatomy* [*Amer. J. Anat.*] **89**, 135–187, Sept., 1951. 22 figs., bibliography.

This paper presents an analysis of reported cases of deficiencies or duplications of long bones. Those most commonly affected are the fibula, radius, femur, tibia, ulna, and humerus. (The clavicle is not included in this study.) Hemimelia may be classified as paraxial (radial, ulnar, tibial, or fibular) or transverse. Paraxial hemimelia is most commonly unilateral, right-sided, and is more often seen in males than females.

Radial hemimelia is, in more than 80% of cases, associated with absence of the scaphoid, trapezium, and thumb. Intercalary radial hemimelia generally consists of a radiostyloid deficiency, accompanied by hypoplasia or aplasia of the scaphoid, trapezium, and first metacarpal. In some cases aplastic bones replace the thumb, and are unconnected with the rest of the skeleton (*le pouce flottant*). In ulnar hemimelia the pisiform and hamate, and often the triquetral and capitate and some of the ulnar metacarpals, are absent. In tibial or fibular hemimelia individual tarsal bones are usually present. Polymelia characteristically occurs in incomplete separation of monozygotic twins; or in single individuals when the lower limb fails to separate, or when duplication occurs. Ulnar dimelia is generally associated with double radial hemimelia. The characteristic morphological patterns occurring in limb deficiencies and duplications is dependent upon successive longitudinal development of the embryonic vertebrate limb.

Peter Ring

1116. **Heredity and Diabetes**
E. M. WATSON and M. W. THOMPSON. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **18**, 326–330, Nov., 1951. 25 refs.

The literature concerning the genetical factors in diabetes mellitus is briefly reviewed. The results of a survey of 4,631 sibs of diabetic propositi are presented. Where neither parent was diabetic some 7·7% of the sibs were affected, and where one parent was diabetic some 15·3% of the sibs were diabetic. No details of the age distributions are given. Although there was a slight excess of like-sexed over unlike-sexed pairs of diabetic sibs, the difference was not significant.

Harry Harris

1117. **Hereditary Ataxia. A Survey of Certain Clinical, Pathologic and Genetic Features with Linkage Data on Five Additional Hereditary Factors**
J. W. SCHUT. *American Journal of Human Genetics* [*Amer. J. hum. Genet.*] **3**, 93–110, June, 1951. 1 fig., 18 refs.

The genetical features of a large family segregating for a form of hereditary ataxia are presented. The clinical and pathological details of these patients have been given elsewhere. The family consisted of 343 individuals in 6 generations, and the disease appeared to segregate as a typical Mendelian heterozygous character. The children of affected individuals were in the ratio of 37 affected to 35 unaffected, which was in good agreement with the 1 to 1 ratio expected theoretically. Some suggestion of " partial sex linkage " was noted, but the effect was not statistically significant.

The age at onset varied from 17 to 40 years, with a mean age of 26·5 years. In 21 instances where both the age at onset and the age at death were known the average duration of the disease was $10{\cdot}2 \pm 4{\cdot}6$ years. The average age at death in 27 cases was $36{\cdot}8 \pm 6{\cdot}4$ years. There was little or no sib–sib or parent–child correlation with respect to age at onset.

An extensive linkage study was carried out in which the blood-group systems ABO, Rh, MN, and Kell were used as " markers ". No indication of any linkage tight enough to be of use for prognostic purposes was found.

Harry Harris

1118. **Studies in Disorders of Muscle—V. The Inheritance of Childhood Progressive Muscular Dystrophy in 33 Kindreds**
F. E. STEPHENS and F. H. TYLER. *American Journal of Human Genetics* [*Amer. J. hum. Genet.*] **3**, 111–125, June, 1951. 6 figs., 11 refs.

The genetics of the syndrome of progressive muscular dystrophy in childhood (or pseudo-hypertrophic muscular dystrophy) is discussed: 33 families involving 1,977 normal and 63 dystrophic individuals are described.

The syndrome in these families appeared to be highly specific. Symptoms started in the third year of life, and by 9 or 12 years of age the children were bed or wheelchair invalids. They usually died from respiratory infection in adolescence or early adult life. The disease was found only in males, and where there was evidence that it passed from generation to generation it was invariably transmitted through the normal female line.

The familial distribution was consistent with sex-linked inheritance, but as the affected males have never had any offspring it is not possible to determine whether the affected males would have been able to transmit the condition to any of their sons. Thus the possibility of an autosomal gene producing the disease in heterozygous males, but not in heterozygous females, could not be excluded. In a number of cases the pedigree configuration was such as to suggest the fairly recent occurrence of a mutation. A rough estimate of the mutation rate in this population gave a figure as high as $9{\cdot}5 \times 10^{-5}$.

Harry Harris

Physiology and Biochemistry

1119. **Observations on a "Fasting Man" during a 53-day Fast.** (Beobachtungen wahrend einer 53tägigen Hungerperiode an einem Hungerkünstler)
U. KANZOW. *Deutsches Archiv für Klinische Medizin* [*Dtsch. Arch. klin. Med.*] **198**, 698–705, 1951. 1 fig., 18 refs.

This paper gives an interesting description of investigations carried out on a man who undertook a 53-day fast in a glass case for pecuniary considerations. During this period only cigarettes and mineral water were supplied. Apart from an expected loss of weight there was surprisingly little change in any of the measurements, which included the serum protein level (with electrophoretic analysis), erythrocyte sedimentation rate, liver function tests, estimation of haemoglobin, haematocrit, and mean erythrocyte diameter, and erythrocyte, leucocyte, and reticulocyte counts. *G. S. Crockett*

1120. **A Histological Contribution to the Study of Vitamin C_2.** (Apport de l'histophysiologie à l'étude de la vitamine C_2)
M. GABE and J. L. PARROT. *Presse Médicale* [*Pr. méd.*] **59**, 1740–1744, Dec. 25, 1951. 23 figs., 27 refs.

Vitamin C_2 is the name given by the authors to the "second antiscorbutic factor" of Randoin, Lecoq, and Bezssonoff, and Szent-Györgyi's "vitamin P". Experiments on rats and guinea-pigs are described, which demonstrate the complementary actions of vitamin C_2 and ascorbic acid. In the latter animal the administration of ascorbic acid alone (10 mg. a day) or of vitamin C_2 alone (3 mg. a week) does not prevent scurvy, whereas their simultaneous administration does. In their experiments the authors undertook careful histological studies of bones, pituitary, thyroid, adrenal, liver, salivary glands, and lymphatic tissues. *A. Wynn Williams*

1121. **Effects of the Intravenous Administration of Gelatin Solution (10%). A Laboratory Study on 24 Patients with Chronic Disease**
R. D. SCOTT and J. RYAN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **222**, 686–696, Dec., 1951. 45 refs.

In an investigation at the City Hospital, Cleveland, Ohio, 500 ml. of 10% solution of gelatin was injected intravenously into 24 chronically ill patients with malnutrition, liver dysfunction, and oedema. The gelatin disappeared rapidly from the blood, only 0·1 g. per 100 ml. or less remaining after 48 hours. Less than one-third of the quantity injected was excreted in the urine in 48 hours. The haematocrit level remained low for 6 hours after the injection, but returned to the pre-injection level in 24 hours. Plasma volume and total blood volume were increased immediately after the injection, and striking increases in urinary volume after 24 hours were more apparent in patients with renal oedema than in those with cirrhosis and ascites. Total protein and non-protein nitrogen content and cephalin–cholesterol flocculation and bromsulphalein retention reactions were unchanged.

The authors suggest that further metabolic studies with intravenous gelatin are indicated, especially in the treatment of nephrotic patients. *I. Ansell*

1122. **Hepatic Blood Flow and Carbohydrate Changes in Man during Fainting**
A. G. BEARN, B. BILLING, O. G. EDHOLM, and S. SHERLOCK. *Journal of Physiology* [*J. Physiol., Lond.*] **115**, 442–455, Dec. 28, 1951. 6 figs., 25 refs.

Fainting was induced in 6 subjects by the application of venous occlusion cuffs to the thighs, with or without venesection in addition. In 2 other subjects spontaneous fainting was studied. By means of the hepatic vein catheterization technique the changes in hepatic blood flow and glucose output and in capillary blood glucose and lactate levels and splanchnic oxygen consumption resulting from fainting were studied. During the period of haemorrhage splanchnic vasoconstriction and diminished blood flow occurred. When fainting supervened decreased blood flow occurred, but there was apparent splanchnic vasodilatation. This was followed by a further period of splanchnic vasoconstriction. Splanchnic blood flow remained low after the systemic blood pressure had returned to normal. Hepatic glucose output and capillary glucose concentration increased at the time of fainting, and peripheral and hepatic venous blood lactate concentrations increased after fainting. During fainting, hepatic venous blood oxygen content diminished greatly. Since the splanchnic blood flow decreased at the same time, the splanchnic oxygen consumption was apparently maintained. *R. A. Gregory*

1123. **Orthostatic Changes of the Pulmonary and Peripheral Circulation in Man. A Preliminary Report.** [In English]
H. LAGERLÖF, H. ELIASCH, L. WERKÖ, and E. BERGLUND. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **3**, 85–91, 1951. 3 figs., 8 refs.

By means of a catheter inserted into the right auricle and later passed into the pulmonary artery, and of an indwelling Cournand needle inserted into the right brachial artery, observations were made on the pressure changes in the pulmonary and systemic circulation in 2 human subjects on tilting from the prone position to an angle of 30 to 60 degrees. All pressure measurements were made at the level of the subject's heart in both positions.

It was found that the systolic brachial blood pressure decreased in the erect position, whereas the diastolic pressure rose markedly and the peripheral resistance in-

creased. On return to the horizontal the reverse changes occurred in a few seconds and 2 minutes respectively in the 2 subjects, and the mean arterial pressure fell to less than the initial value. The pulmonary venous mean pressure fell during tilting and then remained constant or increased slightly; the pulmonary arterial mean pressure also fell slightly. There was an increase of heart rate on tilting, and the stroke volume varied inversely with the rate. The initial decrease in stroke volume during tilting was, however, greater than the increase in heart rate, resulting in a 30% decrease in cardiac output. The pulmonary resistance increased to double its initial value or even more. The right auricular pressure behaved in a similar manner to the pulmonary venous pressure.

These findings are related by the authors to hydrostatic dilatation of the veins in the lower part of the body, to the reduction of pressure in the carotid sinus, and to the fall in intrathoracic pressure due to the lowering of the diaphragm on tilting. *R. P. Foggie*

1124. **Observations on the Temperature of the Human Rectum**

J. GRAYSON. *British Medical Journal* [*Brit. med. J.*] **2**, 1379–1382, Dec. 8, 1951. 4 figs., 14 refs.

In experiments carried out at the University of Bristol blood-flow changes in the human rectum were recorded by means of a heated thermocouple device, and the rectal temperature was measured with copper-constantan thermocouples. Application of cold to the body surface caused an increasing rectal blood flow, accompanied by a rise in rectal temperature; these effects were not affected by occlusion of the venous return from the legs. When the exposed surface of the body was covered with blankets, rectal temperature and blood flow decreased. Intravenous infusion of adrenaline (5 μg. per minute for 5 minutes) produced a fall in rectal blood flow accompanied by a decrease in rectal temperature. It is concluded that intestinal blood-flow changes can cause changes in rectal temperature analogous to changes in skin temperature produced by alterations in cutaneous blood flow. *A. Schweitzer*

1125. **Physiological Analysis of the Relation of Changes in Blood Pressure to Anaemia of the Central Nervous System.** (Физиологический анализ механизма колебаний кровяного давления, возникающих при анемии центральной нервной системы)

A. L. BISOV and G. D. SMIRNOV. *Физиологический Журнал СССР* [*Fiziol. Zh.*] **37**, 621–631, 1951. 6 figs., 29 refs.

Anaesthetized rabbits were subjected to a controlled increase of intracranial pressure by means of Ringer's solution introduced into the subdural space under pressure. It was found that an increase in the intracranial pressure leads to a corresponding increase of blood pressure (after a short period of depression) such that the new level is 20 to 40 mm. Hg higher than the intracranial pressure. This remains true until the intracranial pressure reaches the maximum possible figure for the blood pressure (for the rabbit it is 220 to 250 mm. Hg). If the Ringer's solution is administered intermittently so as to raise the intracranial pressure slowly, step by step, a level is reached at which each subsequent elevation of pressure is followed, not by a steady and definite increase in blood pressure, but by a sequence of waves with a maximum amplitude of from 30 to 100 mm. Hg and a frequency of 3 to 5 a minute. The level of the intracranial pressure at which this phenomenon begins varies with the individual, the number of previous manipulations, and the depth of narcosis. Under deep anaesthesia these waves are abolished.

Polarographic determinations of oxygen content in living brain tissue were made simultaneously with recordings of changes in blood pressure. Oxygen content showed oscillations similar to those of the blood pressure, but of smaller amplitude, and separated from the latter by a definite time interval. There was no relation between these waves and the respiratory rhythm.

Experiments with electrical stimulation of the " sino-carotid zones " and of the depressor nerve, and with the denervation of the " sino-carotid zones ", convinced the authors that the above-described oscillations in the blood pressure and oxygen content in response to a graded rise in intracranial pressure largely depend upon the interaction of the antagonistic pressor (sympathetic) and depressor impulses affecting the vasomotor centre.

The authors regard their work as a further proof of the reflex control of the nervous centres, and argue against the " unscientific " conception of a spontaneous rhythmic activity of these centres. *A. Swan*

1126. **Prothrombin Conversion Factors in Blood Coagulation**

C. A. OWEN, T. B. MAGATH, and J. L. BOLLMAN. *American Journal of Physiology* [*Amer. J. Physiol.*] **166**, 1–11, July 1, 1951. 1 fig., 29 refs.

From estimations of prothrombin and its conversion factors in various preparations of serum and plasma and in various mixtures of these preparations it is concluded that two non-prothrombin substances act as prothrombin conversion factors: one a labile factor which tends to disappear from plasma or serum on standing, and the other a stable factor which is unaffected by storage at 37° C. The labile factor is not obviously reduced in dicoumarol plasma or by Seitz-filtration of oxalated plasma. The stable factor is readily adsorbed by Seitz-filtration and is reduced in dicoumarol plasma. Evidence obtained by adding purified prothrombin in varying proportions to normal plasma suggested that the conversion rate was independent of the prothrombin concentration, but referable directly to the concentration of the accessory factors. *A. Brown*

1127. **Diuretic Effect of Isotonic Saline Solution Compared with that of Water. Influence of Diurnal Rhythm**

G. BLOMHERT, J. GERBRANDY, J. A. MOLHUYSEN, L. A. DE VRIES, and J. G. G. BORST. *Lancet* [*Lancet*] **2**, 1011–1015, Dec. 1, 1951. 4 figs., 27 refs.

This work from the University of Amsterdam sheds some light on two rather neglected forms of diuresis—nocturnal and saline diuresis. Experiments were con-

ducted on healthy men (mostly students) who were kept in a uniform environment and on a uniform and constant food and fluid intake both during the preliminary control period and during the experiment. Diuresis was evoked by giving 2 litres of fluid, evenly distributed throughout an interval of 1 hour, orally or intravenously.

The results of 5 experiments on water diuresis during the day agree with those of previous workers. The diuresis began within the first half-hour after the start of drinking, and excretion of all the excess fluid taken (2 litres) was complete within 4 hours. The urinary levels of sodium, chloride, and potassium fell steeply, as did also, after the first hour, their total output. The blood plasma invariably showed a slight fall in the concentration of chloride and bicarbonate, but the haemoglobin level remained unchanged, so that there was no appreciable blood dilution.

In a study of water diuresis during the night 4 experiments were carried out in which fluid was taken between 11 p.m. and midnight. The diuretic response was retarded, starting in the second half-hour and reaching its peak only after 1½ hours. As a consequence of partial retention of the administered fluid there was a significant dilution of all body fluids, as shown by the fall in the levels of haemoglobin, chloride, bicarbonate, and sodium. An average of only 70% of the water ingested was excreted in 4 hours.

Saline diuresis during the day (the diphasic response) was studied in 20 experiments. Effects resembled water diuresis for the first 1½ hours. After that time, however, the water output decreased to an amount only a little higher than that in the control period, and the excretion of sodium and chloride increased, though that of potassium remained low. Only 1,104 to 2,000 ml. was excreted in 4 hours. The fall in the blood levels of haemoglobin and total protein was always well marked. Slightly hypertonic saline solutions produced the same diuretic response. The above unexpected results cannot be explained by any difference in the rate of absorption of water and sodium chloride, for identical response was obtained after administering isotonic fluid intravenously (4 experiments).

Finally, saline diuresis during the night was studied. After the saline had been drunk (4 experiments) the total output of sodium, potassium, and chloride was remarkably constant, although only 632 ml. of the 2,000 ml. ingested was excreted in 4 hours. After intravenous administration of saline (3 experiments) there was practically complete retention of the fluid given, and consequently a large fall in the haemoglobin and total protein levels of the blood; the rise in the level of the electrolytes was only slight. According to the authors "this must be an important factor in the development of cardiac asthma in patients with slight heart failure".

Of the four types of diuretic response described, the diphasic response is said to be the most characteristic. The first stage is probably due to a sudden decrease in the release of the antidiuretic hormone of the pituitary, which persists until the rise in level of the blood electrolytes becomes sufficiently pronounced to stimulate its secretion.

A. Swan

1128. **Noradrenaline and the Suprarenal Medulla**
D. M. SHEPHERD and G. B. WEST. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **6**, 665–674, Dec., 1951. 4 figs., 23 refs.

Adrenal glands were obtained soon after death from human cadavers of several age groups, and from cats, dogs, rabbits, and guinea-pigs. The glands were extracted with acid saline, and the content of adrenaline and of noradrenaline was estimated by paper chromatography and by biological assay. The results from the two methods were in agreement. In the embryonic adrenal medulla, as in phaeochromocytoma tissue, noradrenaline definitely predominates in amount, and would appear to constitute about 90% of the catechol content in infants. In the adrenal gland of the adult adrenaline constitutes a much larger, but varying, proportion of the active content—about 87%, in adult patients who have died of infection or debilitating disease, of a total activity of 0·24 mg. per g. of whole gland. There is every reason to believe that in fresh glands from individuals who have not died of exhaustion or intoxication the activity would be about four times as much. In adult guinea-pigs and rabbits, in which the ratio of adrenal cortex to adrenal medulla is greater than in other mammals, the content is almost entirely adrenaline. In fowls, in which the ratio of cortex to medulla does not alter after the age of 3 months, the adrenaline–noradrenaline ratio also does not alter. The authors suggest that there is a causal relationship between these observed facts.

James D. P. Graham

1129. **Influence of Thyroid Status on Spermatogenesis**
M. MAQSOOD. *Science* [*Science*] **114**, 693–694, Dec. 28, 1951. 3 figs., 5 refs.

1130. **Regulation of Secretion of Adrenotropic and Thyrotropic Hormones after Stalk Section**
R. J. BARRNETT and R. O. GREEP. *American Journal of Physiology* [*Amer. J. Physiol.*] **167**, 569–575, Dec. 1, 1951. 8 figs., 23 refs.

Section of the pituitary stalk was performed in adult female albino rats by the parapharyngeal approach. This was followed by shrinking, fibrosis, and loss of chromophobe cells in the pituitary, and atrophy of the adrenal and thyroid glands and of the gonads. Growth was also impaired. Dissection and serial section of ink-injected microscopical preparations showed no evidence of portal blood-vessel regeneration. Exposure of the animals, together with normal controls, to a temperature of 3° C. for 7 days resulted in an increase in the output of adrenocorticotrophic and thyrotrophic hormones in both groups, as shown by histological changes in the adrenal and thyroid glands. This would appear to indicate a normal pituitary response to stress, despite the absence of direct neural or vascular connexions with the central nervous system.

The authors conclude from this investigation that the titre of cortical and thyroid hormones in the blood appears to play the major role in regulation of pituitary adrenocorticotrophic and thyrotrophic activity.

Norval Taylor

Pharmacology and Therapeutics

1131. **Physiological and Pharmacological Aspects of Intra-arterial Therapy.** (Quelques aspects physio-pharmacologiques de la thérapeutique par voie artérielle) J. GARRETT. *Journal de Chirurgie* [*J. Chir., Paris*] **67**, 854–868, Dec., 1951. 14 figs., 23 refs.

The chief advantage of injecting a drug into an artery is that it arrives at the desired goal more quickly and in maximum concentration. The physiological effects of intra-arterial injection have not been fully investigated hitherto.

The author investigated in dogs the concentration in the blood of a drug given by arterial injection and found, using a 12% solution of " pentalom " (a sulphur derivative), that even with a considerable dose of the drug injected intra-arterially, most of it seemed to remain in the local tissues and very little to enter the general circulation. He next investigated the relative toxicity of a drug (chloroform) when injected intravenously and intra-arterially. It was found that it needed a greater dose to kill an animal when the drug was given intra-arterially. This was in keeping with the fact that less of the drug reaches the general circulation when it is given intra-arterially.

The local vasomotor effects were also studied after the injection of various substances intra-arterially. There was usually a temporary constriction of the artery which soon passed off; the main feature was a more lasting dilatation of the capillary network; these phenomena were slight with physiological saline, distilled water, pentalom, and penicillin, greater with sulphonamide, still greater with mercurochrome, and greatest of all with hypertonic saline. Procaine caused an immediate vasodilatation. The author considers that the vasodilatation may be one of the factors responsible for the beneficial effect of intra-arterial injection of drugs in certain infections.

Zachary Cope

1132. **Metabolism of N-Acetylsalicylamide. Urinary Elimination of N-Acetylsalicylamide in Normal Man.** (Métabolisme de la N-acétylsalicylamide. Élimination urinaire de la N-acétylsalicylamide chez l'homme normal) P. RAYET, S. BALOUEFF, P. BRUCKNER, and E. PHILIPOTT. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **88**, 159–202, Nov. 1, 1951. 9 figs., 40 refs.

N-Acetylsalicylamide, which has been used clinically in the treatment of rheumatism, is an antipyretic and is well tolerated. When given orally to healthy subjects doses of 10 g. had no unpleasant effects apart from some light-headedness and reddening of the face (like that due to alcohol), more noticeable when little or no food had been taken before its administration. There was no evidence of accumulation after repeated doses of 1·5 g. every 12 hours. From 60 to 95% of a single dose of 1·5 to 10 g. was excreted by the kidneys, mostly during the first 8 hours and all within 24 hours. Most of it was excreted as conjugated salicylamide (35 to 40%) or conjugated salicylate (45 to 50%); 10 to 15% appeared as free salicylamide, 1% as free salicylic acid, and 1% as gentisic acid and amide. There was a notable diuresis about 2 hours after taking the high doses. The conjugated forms were either sulphates or glucuronates, the relative proportions of these varying widely. The sulphate excretion was not directly related to the dose of drug taken or to the concentration in the urine, but the curve of glucuronate excretion followed closely that of elimination of acetylsalicylamide.

The observed changes in sulphate metabolism appear to be indirect and resemble those seen after injection of ACTH. It is considered possible that N-acetylsalicylamide may stimulate the pituitary gland.

Derek R. Wood

1133. **The Action of Barbiturates on Gastric Motility in Human Subjects**
A. G. MELROSE. *Glasgow Medical Journal* [*Glasg. med. J.*] **32**, 244–248, Aug., 1951. 1 fig., 11 refs.

" Seconal " (sodium propylmethylcarbinylallyl barbiturate), 0·2 g., was given through a fine-bore stomach tube to 15 healthy subjects and their gastric movements were recorded for an average period of 60 minutes by means of a rubber balloon connected with the tambour of a kymograph by a second tube. In those patients who remained awake no change in gastric movements occurred. In those who slept, stomach movements ceased for a time in fasting subjects, but returned before waking. In one non-fasting subject no change in movements occurred, although sleep was produced.

V. J. Woolley

1134. **Clinical Evaluation of Methantheline (Banthine) Bromide in Gastroenterology**
G. G. MCHARDY, D. C. BROWNE, F. H. MAREK, R. MCHARDY, and S. WARD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1620–1626, Dec. 22, 1951. 6 refs.

Methantheline bromide (" banthine ") is a drug which has recently been much used in the treatment of gastro-intestinal disorders, its effects and action being anti-cholinergic. This is a report, from the Browne–McHardy Clinic in New Orleans, on the use of the drug in healthy subjects and in a variety of clinical conditions; studies of the effects of banthine were controlled by parallel administration of atropine, " bentyl " (β-diethylaminoethyl-1-*cyclo*hexyl*cyclo*hexane-carboxylate) hydrochloride and placebos. Salivary and gastric secretory volume was reduced by banthine, but the titratable free acidity of the gastric contents was little altered except in patients with chronic intractable duodenal ulcer. In the few patients tested banthine

diminished pancreatic and ileal secretions, but did not lessen diarrhoea in cases of regional enteritis and ulcerative colitis. The drug inhibited gastric motility, but exaggerated any tendency towards cardiospasm. The gastro-colic reflex was inhibited.

There was no significant effect on rate of healing in duodenal ulcer, regional enteritis, or ulcerative colitis, but the drug induced relief of pain, particularly nocturnal pain, in the majority of cases of duodenal ulcer tested.

[This paper is very well documented and should be read in the original by those wishing to try banthine in any gastro-intestinal disorder.] *J. Naish*

1135. **Interdigestive Gastric Secretion in Duodenal Ulcer. A Study of the Comparative Inhibition by Hexamethonium Iodide and L-Hyoscyamine**
M. J. RIDDELL. *British Medical Journal* [*Brit. med. J.*] **2**, 1498–1500, Dec. 22, 1951. 1 fig., 16 refs.

In a study carried out at the Western General Hospital, Edinburgh, the author compared the effect of hexamethonium iodide with that of L-hyoscyamine or tincture of belladonna on interdigestive gastric secretion in 5 male patients with duodenal ulcer. During a 10-hour period starting at 9 p.m. the stomach contents were aspirated continuously by means of a Ryle's tube and an electric pump (radiographic confirmation of the position of the Ryle's tube being found to be essential). Collections were made hourly and the samples placed in a refrigerator until the following afternoon, when the volume, free and total acidity, and peptic activity of each hourly sample was recorded.

The hyoscyamine or belladonna was given orally at 8 p.m., the dose being the minimum which was found to produce a dry mouth and blurred vision on waking next day. This dose, which happened to be the same in all subjects, was 0·07 grain (4·6 mg.) of L-hyoscyamine (4 patients) or 210 minims (12·6 ml.) of tincture of belladonna, containing approximately the same amount of hyoscyamine (one patient). Hexamethonium iodide was given by intramuscular injection at 9 p.m., midnight, and 3 a.m., each dose being 100 mg.

The effect of each drug was expressed as the percentage reduction produced in the mean hourly values as determined in control collections under identical conditions before and after those in which the drugs were given. The reduction in volume of juice and free and total acidity produced by hexamethonium and hyoscyamine was of the same order in each case. Hexamethonium had a greater effect than hyoscyamine on the output of pepsin in all but one case, but the difference was not statistically significant in so small a series. There was notable agreement between the mean control values obtained before and after giving the drugs.

There were few complaints of side-effects, although one patient had a disturbing headache after hyoscyamine and orthostatic hypotension after hexamethonium. It is pointed out that the use of hexamethonium intramuscularly should be limited to hospital treatment, while the doses of belladonna given were larger than those normally used, being given rather early in the evening. For therapeutic purposes smaller doses, given later, should suffice to produce the dry mouth and mydriasis next day and to reduce the interdigestive secretion.

[This interesting and careful study reaffirms the effectiveness of belladonna when given in adequate doses. In view of the recent interest in the new drug " banthine " for the treatment of duodenal ulcer, it would be instructive to compare its effect with that of belladonna or hyoscyamine by the same method. Certain American reports suggest that banthine has little more to offer than atropine or belladonna. Its ganglionic blocking action is probably not very important.] *Derek R. Wood*

1136. **The Action of the Local Hormones on the Isolated Human Bronchus.** [In English]
L. M. ROSA and R. J. S. MCDOWALL. *Acta Allergologica* [*Acta allerg., Kbh.*] **4**, 293–304, 1951. 9 figs., 27 refs.

This paper on the reactions of isolated human bronchi comes from the Department of Physiology, King's College, University of London.

Human quaternary bronchi, obtained during operation, were left in a vacuum flask containing Krebs's solution at 37·5° C. The bronchus was dissected as a spiral or chain for kymographic study of the action of various drugs. For 1 or 2 hours after death there was an increased tonus, probably due to histamine production induced by the dissection. It was found in such a preparation that histamine and acetylcholine caused a contraction and adrenaline a marked relaxation, whereas the effect of ephedrine was less active but more lasting than that of adrenaline. Atropine antagonized the action of acetylcholine, as was histamine contraction by various antihistaminic drugs. A bronchus from a flour asthmatic gave a specific contraction when treated with flour-dust extract.

It is concluded that isolated human bronchi give reactions like those of a guinea-pig rather than those of a rat or rabbit. *A. W. Frankland*

1137. **Acetylcholine and Respiration.** [In English]
G. LILJESTRAND. *Acta Physiologica Scandinavica* [*Acta physiol. scand.*] **24**, 225–246, Dec. 8, 1951. 12 figs., 22 refs.

1138. **Effect of Veratramine on Arterial Pressure and Heart Rate in Normal and Hypertensive Dogs**
J. W. MCCUBBIN and I. H. PAGE. *American Journal of Physiology* [*Amer. J. Physiol.*] **167**, 714–720, Dec. 1, 1951. 2 figs., 11 refs.

The effects of veratramine acetate on the blood pressure and heart rate of normal dogs and dogs with renal and with chronic neurogenic hypertension were studied. Neurogenic hypertension was produced by bilateral excision of the carotid sinuses, section of one sympathetic depressor trunk, and the other entire vago-sympathetic-depressor trunk in one operation (Grimson, *Arch. Surg.*, 1941, **43**, 284). Animals were not used unless they had a well-sustained hypertension of 200 mm. Hg or more, blood pressure being measured by direct puncture of the femoral artery. Renal hypertension was elicited by

inducing a "cellophane" perinephritis. Cardiac sympathectomy was accomplished by bilateral removal of the thoracic sympathetic chains from, and including, the stellate ganglion to the 9th rib. The veratramine acetate was made up in 12% ethyl alcohol and diluted with distilled water to give a solution containing 1·15 mg. per ml. The dose was either 0·1 or 0·2 mg. per kg. body weight calculated as the base, and was given by femoral vein.

Normal and renal hypertensive animals responded similarly to veratramine with slight to moderate reductions in arterial pressure and heart rate. In sharp contrast, veratramine caused marked hypotension in neurogenic hypertensive dogs. In 9 normal dogs the average fall was 13 mm. Hg, whereas in the same dogs after the induction of chronic neurogenic hypertension the average vasodepressor response was 71 mm. Hg. The response of the latter was not affected by cardiac sympathectomy, although this prevented slowing of the heart; during the hypotensive response stroke volume and minute volume increased, indicating diminished peripheral resistance. Autonomic blockade by tetraethylammonium chloride reduced the response of neurogenic hypertensive dogs to veratramine, but the response was unaltered by bilateral vagus section or atropine. Clonic convulsions were often induced by a dose of 0·1 mg. per kg. and were almost invariably induced by larger doses.

It is concluded that veratramine lowers the arterial pressure, largely by decreasing peripheral resistance, the decrease being mediated by the sympathetic nervous system, and that its activity does not depend on decreased cardiac rate or output. *Norval Taylor*

1139. **Regulation of Blood Pressure Levels by Hexamethonium Bromide and Mechanical Devices**
P. A. RESTALL and F. H. SMIRK. *British Heart Journal* [*Brit. Heart J.*] **14**, 1–12, Jan., 1952. 8 figs., 27 refs.

In the investigation described, which was carried out in the University of Otago, Dunedin, New Zealand, the circulatory effect of hexamethonium bromide (HMB) in man was studied by plethysmographic and ballistocardiographic methods. The apparatus used made it possible to apply both negative and positive pressure to the lower two-thirds of the body. In hypertensive subjects, whether in failure or not, an injection of HMB produced a fall in venous pressure in some cases before the arterial pressure had decreased. Postural hypotension was fully investigated.

The authors conclude that HMB alters the relationship between cardiac output and peripheral resistance, so that for any given cardiac output the peripheral resistance is less than it would be in the absence of HMB. This altered situation is not abolished by emotion, mild exercise, or meals. Postural hypotension induced by HMB can be shown in both the horizontal and the vertical posture, and appears to be dependent upon a decrease in the power of the vessel walls in dependent parts to contract and resist gravity-pressure dilatation. This may result from less effective action of the sympathetic paths. *James W. Brown*

1140. **The Influence of Dihydroergotamine Methanesulfonate (DHE-45) on Epinephrine-induced Cardiac Irregularities in Dogs during Anesthesia with Several Agents.** [In English]
J. M. WHITE, M. H. NOLTENSMEYER, and L. E. MORRIS. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **88**, 361–367, Dec. 1, 1951. 13 refs.

Partial or complete protection was given by 0·2 mg. of dihydroergotamine methanesulphonate (DHE-45) per kg. body weight against cardiac arrhythmia of ventricular origin produced by adrenaline injection in dogs anaesthetized with chloroform, ethyl chloride, trichlorethylene, or cyclopropane. The dose of DHE-45 was diluted to 5 ml. and given slowly by intravenous injection during 50 seconds. Its protective effect was found to be adequate after 15 minutes and to last for 1 to 2 hours, and it is therefore suggested that dihydroergotamine might be useful in the premedication of a patient subject to such cardiac sensitization. *Derek R. Wood*

1141. **The Pharmacologic Action of Thevetoidin, a Cardioactive Substance Obtained from a Mexican Species of *Thevetia***
R. MÉNDEZ, E. SODI-PALLARES, and A. NAVA. *Circulation* [*Circulation*] **4**, 854–862, Dec., 1951. 5 figs., 16 refs.

Thevetoidin is the name given to a crystalline substance obtained from an alcoholic extract of the seeds of *Thevetia gaumeri*. It consists mainly of a glycoside, but possibly contains small amounts of other substances. Its action is essentially similar to that of the digitalis glycosides. Toxicity in the frog is about 1 in 200, and in the cat about 1 in 20, of that of ouabain. It differs from most cardiac glycosides in the ready reversibility of its effects, and it can be washed out from the isolated frog heart in 30 to 60 minutes after complete systolic arrest has been brought about. In the heart–lung preparation of the dog, heart failure caused by pentobarbitone is abolished by 0·8 mg. of thevetoidin, the effect lasting 50 to 70 minutes. Its effects on the vagus and in the causation of nausea and diarrhoea are greater than those of most other cardiac glycosides. A dose of 10 mg. is recommended for clinical use.
V. J. Woolley

1142. **The Action of Several Cardiac Glycosides on Conduction Velocity and Ventricular Excitability in the Dog Heart**
G. K. MOE and R. MÉNDEZ. *Circulation* [*Circulation*] **4**, 729–734, Nov., 1951. 4 figs., 9 refs.

In experiments at the National Institute of Cardiology, Mexico, digitoxin, ouabain, K-strophantoside, and lanatoside C were administered to dogs under chloralose anaesthesia in order to compare their action on ventricular excitability, auriculo-ventricular interval, ventricular conduction, and idioventricular activity. The drugs were administered at 30-minute intervals in doses estimated to be 12 to 16% of the acute lethal dose. With each drug an initial slight increase in ventricular excitability occurred, which declined progressively after 60 to 80% of the lethal dose had been given. Ventricular

ectopic beats appeared after the injection of 40 to 60% of the lethal dose. At this point ventricular excitability was only slightly increased. Ectopic beats became more frequent when the excitability of the ventricle was, on the average, less than 70% of the normal, thus demonstrating that the implication that idioventricular activity develops because the irritability of the ventricle is increased is invalid. It is emphasized that the error is one of terminology.

The auriculo-ventricular interval was prolonged with all agents, complete block occurring after 65 to 75% of the lethal dose had been given. Digitoxin and lanatoside C caused auriculo-ventricular block earlier than the strophanthus glycosides, but the significance of these findings is considered questionable in view of the small number of the experiments.

Conduction rate was well maintained within the ventricle with 50 to 60% of the lethal dose for all the glycosides, after which slowing occurred progressively. No depression of the conduction rate was found between the stimulating electrodes and a close recording electrode, where the path must have been mainly muscular, whereas depression was most marked where the conduction pathway must have included Purkinje tissue.

On the whole no significant differences in effect were observed between the glycosides.

Catherine Schopflin

1143. ***In vitro* Studies of the Coronary Arteries of Man and Swine as Demonstrated by a New Technic, Angioplethysmokymography**

D. J. SMITH, J. T. SYVERTON, and J. W. COXE. *Circulation* [*Circulation*] **4**, 890–898, Dec., 1951. 5 figs., 41 refs.

The authors review previous methods used to measure responses of blood vessels to various stimuli, and consider their deficiencies. None of the methods fulfil the dual requirements which they consider essential, namely: (1) that the vessels remain intact as to their constituent layers; and (2) that they be uninfluenced by extravascular stimuli. They then describe a method that fulfils these criteria. The segment of artery to be studied is contained in a plethysmographic chamber containing Tyrode's solution modified to contain 0·2% sodium bicarbonate, with a *p*H of 7·4, the oxygen concentration being 2 volumes % and the carbon dioxide concentration 55 to 60 volumes %. The artery is mounted at each end on cannulae that pierce the chamber, one communicating via a warming coil with a reservoir and the other an outflow. Technical refinements allow for perfusion of the artery with various solutions under constant conditions of pressure, oxygenation, and rate of flow, the maintenance of constant temperature, and photographic recording of changes in volume of the arterial segment per unit of time. Coronary arteries were obtained as soon after death as possible from healthy swine and young human adults, and segments were mounted in the plethysmographic chamber. Perfusion with histamine consistently caused vasoconstriction, and antihistaminic drugs were shown to block this vasoconstrictive action. Similarly acetylcholine had a vasoconstrictive effect that could be blocked by atropine. In coronary artery segments that had assumed a certain degree of tone with standard perfusate, vasodilator effects could be produced with L-adrenaline and L-noradrenaline. An interesting suggestion is made that combined therapy with atropine and antihistaminic drugs might be useful in treatment of disease states associated with evidence of reflex coronary artery spasm.

K. G. Lowe

1144. **Clinical Experiences with 4-Hydroxycoumarin Anticoagulant No. 63 and the Antagonistic Effect of Menadione and Vitamin K**

H. H. HANSON, N. W. BARKER, and F. D. MANN. *Circulation* [*Circulation*] **4**, 844–853, Dec., 1951. 5 figs., 9 refs.

4-Hydroxycoumarin anticoagulant No. 63 (of Ikawa *et al.*, *J. Amer. chem. Soc.*, 1944, **66**, 962) has effects similar to those of dicoumarol, but is 2 to 3 times more potent. In studies on 100 patients at the Mayo Clinic the drug was given by mouth and the therapeutic prothrombin level was taken to be that at which the clotting time was approximately doubled. In some cases it caused a fall in blood prothrombin level when dicoumarol had failed. If the clotting time had been excessively prolonged by overdosage with the drug, it could be reduced to a therapeutic level by giving menadione, but not to the previous normal level; it could, however, be reduced to normal by giving vitamin K_1. The prolongation of clotting time persisted for about 8 days after administration ceased if no antagonist was given.

V. J. Woolley

1145. **Bishydroxycoumarin, Ethyl Biscoumacetate, and 4-Hydroxycoumarin Anticoagulant No. 63. Comparative Effects**

N. W. BARKER, H. H. HANSON, and F. D. MANN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 274–277, Jan. 26, 1952. 5 figs., 17 refs.

The effects of dicoumarol given to 100 patients, of ethyl biscoumacetate (" tromexan ") given to 50 patients, and of 4-hydroxycoumarin anticoagulant No. 63 given to 100 were compared. The one-stage method of estimating prothrombin time (Quick) was used throughout, with a dried saline extract of rabbit brain for thromboplastin. Normal prothrombin times with this technique were 18 to 20 seconds, and the desired hypoprothrombinaemia for therapeutic purposes was established at a range of 27 to 58 seconds. Daily measurements were carried out on all patients.

All three agents reduced prothrombin levels. Equieffective doses were 5 to 6 times as much tromexan, and half to one-third as much of No. 63, as of dicoumarol. The schedule used was 300 mg. of dicoumarol on the first day and 100 mg. on the second; of tromexan, 1,500 mg. and 600 to 900 mg.; of No. 63, 100 to 150 mg. and 25 to 50 mg. All drugs were given by mouth in one dose per day. After the second day, estimation of the prothrombin time gave the indication for further dosage. The three compounds were equally effective in appropriate dosage, and the number of toxic reactions, with haemorrhage, was similar for each. Tromexan acted more quickly and for a shorter period, and No. 63

more slowly and for a longer period, than dicoumarol. Under treatment with tromexan stabilization of dosage was more difficult because of variability of the prothrombin time after initial dosage (apart from the extreme variability from patient to patient); this feature was much less prominent with No. 63, but the action persisted much longer after discontinuance of the drug.

Vitamin K was an antidote to all three compounds, but with some differences in detail which are of practical importance. Thus 500 mg. of vitamin K_1 restored the prothrombin time to normal within 24 to 48 hours after dicoumarol or after No. 63, while tromexan is short-lasting in any case and it was doubtful if the vitamin significantly hastened restoration of normal clotting. Menadione sodium bisulphite restored an excessive hypoprothrombinaemia to therapeutic levels rapidly, but was not so effective in restoring it to the normal initial level. Thus the latter agent is preferred for correction of incidental errors during therapy and the former agent for terminating therapy. This difference in effectiveness was particularly evident with anticoagulant No. 63.

James D. P. Graham

1146. **The Hypoprothrombinemia-inducing Activity of Link's Compound 63 (Methopyranorin).** [In English]
S. SHAPIRO. *Acta Haematologica* [*Acta haemat., Basel*] 6, 129–140, Sept., 1951. 6 figs., 7 refs.

In this paper are described trials in man of a new anticoagulant drug—methopyranorin—which, when given by mouth, causes a substantial prolongation of the prothrombin time within 12 to 24 hours after its ingestion. The maximum effect may not be manifest for 72 to 96 hours, and the drug is well suited for administration in properly spaced intermittent doses. An initial dose of 200 to 300 mg. is generally found satisfactory, and second and subsequent doses are determined by the extent of the response observed after the previous dose. The second dose is usually about one-half of the first. Dose for dose, methopyranorin is two to three times as effective as dicoumarol in inducing hypoprothrombinaemia. As in the case of dicoumarol, vitamin K and transfusions of fresh blood promptly counteract this effect of the drug.

Douglas H. Collins

1147. **The Isolated Kidney and its Response to Diuretic Agents**
S. KUPFER, D. D. THOMPSON, and R. F. PITTS. *American Journal of Physiology* [*Amer. J. Physiol.*] **167**, 703–713, Dec. 1, 1951. 6 figs., 12 refs.

In experiments performed at Cornell University Medical College an apparatus for perfusing the isolated kidney of a dog was used in which a valveless pump replaced the heart in the usual heart–lung–kidney preparation. For each experiment 2 dogs were anaesthetized and given large amounts of balanced glucose and salt solution intravenously. The larger animal was heparinized and rapidly bled to death. The lungs were removed within 10 to 15 minutes of bleeding, and perfused for 30 to 60 minutes before connecting the kidney to the apparatus. The blood was oxygenated by intermittent inflation of the lungs with oxygen containing 5% carbon dioxide. One kidney of the smaller dog was dissected free, the renal vessels stripped, the nerves cut, and the ureter catheterized. The animal was primed with creatinine and *para*-aminohippurate (PAH), the plasma levels of these substances being maintained by a constant infusion in the standard manner. After 30 minutes had been allowed for stabilization several clearance estimations were performed. The kidney was then removed and connected to the perfusion apparatus, the blood supply to the kidney being interrupted for less than 3½ minutes. The kidney was then perfused for 20 to 60 minutes before further studies were performed. Creatinine and PAH levels were maintained by infusion into the blood reservoir. Since in all the estimations *in vivo* creatinine clearance exceeded 1·0 ml. per kg. body weight per minute this figure was arbitrarily selected as the minimum acceptable after transfer of the kidney to the pump, although this meant discarding 9 out of 15 results.

On transferring the kidney to the pump there was an invariable reduction in the glomerular filtration rate, and the urine : plasma concentration ratio was generally lower than *in vivo*. The sodium excretion rate fell progressively during perfusion, while that of potassium remained essentially at the initial level. The blood flow through the kidney at comparable pressures was reduced as evidenced by PAH and haematocrit studies, indicating a higher total vascular resistance. The administration of 50 mg. of aminophylline caused a dramatic fall in total renal resistance at constant pressure. Changes in glomerular filtration rate were inconsistent. Diuresis occurred without significant changes in glomerular filtration rate and must therefore be attributed to diminished tubular reabsorption of sodium and water. Mersalyl administered intra-arterially in a dose containing 8 mg. of mercury induced partial or complete renal vascular shut-down and oliguria. This action could be abolished by adding aminophylline to the mersalyl solution. Mersalyl added to the blood reservoir caused a diuresis due to diminished reabsorption of sodium and water.

Norval Taylor

1148. **The Effect of Adrenaline and Noradrenaline on Hepatic Blood Flow and Splanchnic Carbohydrate Metabolism in Man**
A. G. BEARN, B. BILLING, and S. SHERLOCK. *Journal of Physiology* [*J. Physiol., Lond.*] **115**, 430–441, Dec. 28, 1951. 6 figs., 23 refs.

In this study from the Postgraduate Medical School, London, of the effect of adrenaline and noradrenaline on carbohydrate metabolism and hepatic blood flow. hepatic venous blood was obtained by catheter from 22 normal subjects after 12 hours' bed rest and fasting; the liver blood flow was estimated by the bromsulphalein infusion method. Hepatic and systemic venous blood samples were also analysed for glucose, lactate, and oxygen content, and from the results obtained calculations made of the rate of glucose, lactate, and oxygen exchange by the liver.

Intravenous infusion of adrenaline increased hepatic blood flow, oxygen consumption, and glucose output;

the peripheral venous lactate concentration increased. Infusion of noradrenaline slightly decreased hepatic blood flow and slightly increased hepatic glucose output and oxygen consumption. Peripheral venous lactate concentration showed little change. Adrenaline increased the pulse rate and systolic blood pressure, and decreased the diastolic pressure. Noradrenaline decreased the pulse rate and increased systolic and diastolic blood pressure. *R. A. Gregory*

1149. **Mytolon Chloride: a New Agent for Producing Muscular Relaxation. Preliminary Report**
J. G. ARROWOOD. *Anesthesiology* [*Anesthesiology*] **12**, 753–761, Nov., 1951. 1 fig., 10 refs.

" Mytolon chloride " is 2 : 5-bis-(3-diethylaminopropylamino)-benzoquinone-bis-(benzyl) chloride, and was synthesized by Cavallito, Soria, and Hoppe (*J. Amer. chem. Soc.*, 1950, **72**, 2661). It is a red crystalline solid, soluble in water to the extent of 20%. Its potency slightly exceeds that of D-tubocurarine chloride. It causes no significant change in the pulse rate or blood pressure, and 1,500 times the curarizing dose has been given without causing cardiac arrest to dogs receiving artificial ventilation. It has no effect on autonomic ganglia or upon the vagus, though excessive salivation may be caused in patients unprotected with atropine. Muscular relaxation begins within 3 minutes of the intravenous injection, and reaches its height after 12 to 15 minutes; apnoea never lasts longer than 15 minutes with a single dose. The drug is excreted by the kidney, and large doses turn the urine red. The author, who carried out her investigation at the Massachusetts Memorial Hospitals and the Boston University School of Medicine, considers that the chief advantages of the drug are its lack of effect on the cardiovascular system and the prompt recession of respiratory depression. *Gordon Ostlere*

1150. **Variations in Response to Relaxant Drugs**
J. W. DUNDEE and T. C. GRAY. *Lancet* [*Lancet*] **2**, 1015–1018, Dec. 1, 1951. 5 figs., 16 refs.

In this paper from the University of Liverpool are discussed the factors giving rise to hypersensitivity and hyposensitivity to relaxant drugs. A case of myasthenia gravis is described in which the patient was given injections of D-tubocurarine chloride and decamethonium; she proved hypersensitive to the D-tubocurarine chloride (as expected), but her response to decamethonium was within normal limits. Two cases (in patients not myasthenic) of hypersensitivity to relaxants are described, and the importance of a test dose of any relaxant being first administered by the anaesthetist is emphasized. A case of hyposensitivity to relaxant drugs is also described; this patient, following repeated operations, became progressively more resistant to drugs of the curare series. The authors suggest that this increased tolerance to D-tubocurarine chloride may have been due to the large doses of sedatives and analgesics which this patient was taking.

It is demonstrated that the effect of decamethonium on the respiration is reduced in patients who have received previous doses of D-tubocurarine chloride. On the other hand, when D-tubocurarine chloride is given after decamethonium the paralysant effect of the former on respiration is increased. *A. M. Hutton*

1151. **Studies on " Convulsive " Thiobarbiturates**
R. K. RICHARDS. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **30**, 348–353, Nov.–Dec., 1951. 11 refs.

Sixteen 5:5-substituted thiobarbiturates were examined for their hypnotic and convulsant actions in mice, rabbits, and monkeys. The protective effects of the drugs against " metrazol " (leptazol) convulsions in mice were also measured. Eleven of the compounds had substituents consisting of a 1-, 2-, or 3-methylallyl group and an alkyl chain; the other 5 substances contained *n*-butyl, *iso*butyl, or butenyl groups; 2 of them contained chlorine atoms.

In mice the drugs produced a mixture of hypnosis and excitement, sometimes with convulsions. In rabbits almost all of the drugs produced convulsions. On the other hand, except for the *n*-butyl-*iso*amyl and the hexyl-3-chlorobutenyl derivatives, all of the substances caused sleep without excitement in rhesus monkeys. The hypnotic action in monkeys was paralleled in 13 of the 16 substances by their effect in preventing leptazol convulsions in mice.

The author suggests that monkeys should be used more widely for assessing the value of hypnotic drugs, because the results of tests with mice and rabbits may be misleading. *L. G. Goodwin*

1152. **The Effect of Various Barbiturates on the Central Nervous System.** (Olika barbituraters verkan på centrala nervsystemet)
C. M. IDESTRÖM. *Nordisk Medicin* [*Nord. Med.*] **47**, 113–118, Jan. 25, 1952. 8 figs., 10 refs.

The author carried out investigations at the Karolinska Institute, Stockholm, on the effect of single doses of certain barbiturates on the central nervous system in healthy adults, in epileptics under continuous treatment with phenobarbitone, and in patients suffering from chronic barbiturate poisoning and addiction. Flicker-fusion frequency, corneal sensitivity to a jet of air (blink test), and standing steadiness (Romberg's test) as shown by photographic records, were estimated before and after administration of a standard dose (0·3 g. per 70 kg. body weight) of each barbiturate and also of ethyl alcohol, chloral hydrate, and other sedative drugs, and of inert placebos. In some cases these last had a marked suggestive effect in that the subject complained of drowsiness and even fell asleep; however, no effect was observed on the test responses.

All the barbiturates tested had a depressive effect on normal subjects, as revealed by raised threshold values for the blink test and flicker-fusion frequency. This effect became demonstrable 15 minutes after taking " amytal ", increased to a maximum at 150 minutes, then slowly diminished until after 250 to 300 minutes it was no longer measurable; the effect of amytal on Romberg's test was also maximal after 150 minutes. In the early stages the subject felt elated, and loss of judgment similar to that seen in alcoholic conditions was observed;

however, this euphoric stage was followed by a feeling of tiredness and drowsiness. With cyclobarbitone, hexobarbitone, and other barbiturates, however, the effect was nearly maximal after 10 to 15 minutes and remained at this level for 250 to 300 minutes. Sensitivity to pain and touch was significantly reduced, and there was no stage of excitation, drowsiness setting in from the start. The effect of ethyl alcohol on normal subjects was very similar to that of the barbiturates, the author calculating that a dose of 0·31 g. of barbiturate per 70 kg. corresponds to approximately 0·12 to 0·15 litre of spirits. On the other hand chloral hydrate, 1·5 to 2·0 g., had an immediate (5 to 10 minutes) and intense, but transient, effect, lasting 100 to 150 minutes, which was especially revealed by Romberg's test.

In patients with epilepsy the same tests were carried out before, and at intervals during, treatment with daily doses of phenobarbitone. The depressive effect of a standard dose of barbiturate was found to diminish gradually until, after about 2 months, it had a stimulant effect. A similar stimulant effect of barbiturates and also of ethyl alcohol and other drugs was observed in cases of chronic barbiturate poisoning.

E. S. Fountain

1153. **Mode of Blocking of Axonal Activity by Curare and Inhibitors of Acetyl-cholinesterase**

H. GRUNDFEST, D. NACHMANSOHN, C. Y. KAO, and R. CHAMBERS. *Nature* [*Nature, Lond.*] **169**, 190, Feb. 2, 1952. 3 refs.

1154. **Action of Mepyramine on Convulsions due to Leptazol and on Narcosis due to Bromethol.** (L'action du néoantergan sur les convulsions au cardiazol et sur la narcose à l'avertine)

G. ABBOZZO, E. GENAZZANI, and L. DONATELLI. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **88**, 209–222, Nov. 1, 1951. 2 figs., 3 refs.

From the University of Naples the authors report that although the effect of "neoantergan" (mepyramine) on the nervous system varies in different species, it generally has a central depressant action in small doses (0·1 to 1 mg. per kg. body weight) and a convulsant action in high doses (20 mg. per kg.). The type of action is seen more clearly when the substance is given with "cardiazol" (leptazol) or "avertin" (bromethol). Small doses of mepyramine potentiate the narcotic effect of bromethol and antagonize the convulsive action of leptazol, whereas large doses of mepyramine potentiate the action of leptazol and antagonize the effect of bromethol. These effects were obtained in experiments on mice, guinea-pigs, frogs, and carp. The observations fit in with the known sedative effects of many antihistaminics in therapeutic doses and their convulsant effects in toxic doses, especially in children.

[These results confirm earlier findings, and may be of some help in indicating the more suitable forms of drug therapy for antihistaminic poisoning.]

Derek R. Wood

1155. **A Controlled Study of Pain Relief by Intravenous Procaine**

A. S. KEATS and H. K. BEECHER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1761–1763, Dec. 29, 1951. 10 refs.

This is a report on the relief of pain by intravenous procaine made to the Council on Pharmacy and Chemistry of the American Medical Association [which presumably endorses the conclusions]. The study was made in 53 patients on the first day after major surgical operations. When they complained of pain they were treated by the intravenous administration of saline (as a placebo), procaine hydrochloride (the drug under test), or morphine (a well-tried effective drug), and the results were evaluated objectively 30 minutes later. If one drug did not relieve the pain, another was given.

Saline relieved pain in 20%, procaine in 40%, and morphine in 70%. The relief produced by procaine was approximately the same as that produced by 90 mg. of pentobarbitone sodium; apparently it was due to the action of procaine upon the central nervous system and not to a local action. Procaine frequently produced unpleasant side-reactions such as dizziness, nausea, vomiting, numbness, oppressive chest sensation, or tachycardia; sometimes the reactions were serious, resulting in convulsions or disorientation. It is considered, therefore, that in the light of present evidence procaine should not be given intravenously for the relief of pain.

F. Hawking

1156. **Lime Wash with Hexachlorane as an Insecticidal Application for Covering Walls and Ceilings.** (К вопросу о длительности инсектицидного действия мелового побелочного материала с примесью гексахлорана в жилых помещениях)

N. V. GEMINOV. *Гигиена и Санитария* [*Gigiena*] No. 9, 49–50, 1951.

Experiments were performed to determine the insecticidal value of a lime wash containing hexachlorane. Several rooms in a group of flats were used and the walls and ceilings of these were covered with the wash, which was prepared by mixing lime with 5% of hexachlorane, 2% of commercial blue, and 15% of casein glue and adding water so that a semiliquid mass was obtained. Just before use this was diluted to the consistency of milk. It could be applied to an old wall surface without previous preparation, and about 60 g. was needed per square metre. It is recommended that after the wash is applied the rooms should not be used until they are quite dry since fumes are given off.

The preparation was lethal to flies, bugs, cockroaches, and other insects, and when a number of flies were introduced experimentally into a closed room treated with the wash, all died within 15 hours. *G. C. Pether*

1157. **Promising DDT-Synergist Combinations for the Control of Resistant Flies**

W. T. SUMERFORD, R. W. FAY, M. B. GOETTE, and A. M. ALLRED. *Journal of the National Malaria Society* [*J. nat. Malar. Soc.*] **10**, 345–349, Dec., 1951. 13 refs.

1158. **Biting Insects in the Arctic and Sub-arctic**
R. A. SMART. *Journal of the Royal Army Medical Corps* [*J. R. Army med. Cps*] **98**, 8–14, Jan., 1952. 5 refs.

CHEMOTHERAPY

1159. **Protection of Mice against Vaccinia Virus by Administration of Benzaldehyde Thiosemicarbazone**
R. L. THOMPSON, M. L. PRICE, and S. A. MINTON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **78**, 11–13, Oct., 1951. 10 refs.

Using a medium containing minced chick embryonic tissues, the authors found that the growth of the CVII strain of vaccinia virus was completely inhibited (but not inactivated) by the presence of benzaldehyde thiacetazone in a concentration of 1 μg. per ml. of culture medium. Substitutions in the *para* position of the benzene nucleus, or the introduction of an *iso*butyl group in the 4-position of the thiacetazone portion of the molecule, reduced the activity of the compound in all cases.

In experiments *in vivo*, benzaldehyde thiacetazone was more active than any other member of the series tested. In 14 experiments in which it was present in the diet in concentrations varying from 0·02 to 0·08%, 59% of 244 mice survived, in contrast to 16% of 243 control animals. Derivatives with substitutions in the *para* position of the benzene nucleus, or in the 4-position of the thiacetazone portion of the molecule were inactive. *R. Hare*

1160. **Evaluation of Some Chemotherapeutics against *Endamoeba histolytica* in Cultures with *Trypanosoma cruzi***
M. NAKAMURA and H. H. ANDERSON. *Experimental Parasitology* [*Exp. Parasit.*] **1**, 66–69, Oct., 1951. 14 refs.

The recent introduction of bacteria-free cultures of *Entamoeba histolytica* growing in association with *Trypanosoma cruzi* has provided the means of studying the direct action of drugs on the amoebae alone, since *T. cruzi* is known to be resistant to chemotherapeutic agents. The authors record in tabular form the results of tests *in vitro* upon such mixed cultures of the following antibiotics and amoebicidal drugs: aureomycin, actidione, polymyxin, bacitracin, carbarsone, diodoquin, emetine hydrochloride, phenylurea-*p*-di-(carboxy-methyl)-thioarsenite, terramycin, and vioform sol. These results are compared with previous tests on monobacterial cultures of *E. histolytica* growing in cotton-stoppered (" open ") tubes and in tubes which were " sealed " with petrolatum.

It was confirmed that the chemical used had no effect on the associated trypanosome, whereas the amoebicidal end-point ranges corresponded closely to those obtained with the " sealed " monobacterial cultures. Mixed cultures of *E. histolytica* and *T. cruzi* thus provide a method for study of direct amoebicidal action *in vitro* in the absence of concomitant bacteria, which tend to obscure such tests. *C. A. Hoare*

ANTIBIOTICS

1161. **Observations on Antiviral Activity of Viscosin**
V. GROUPÉ, L. H. PUGH, D. WEISS, and M. KOCHI. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **78**, 354–358, Oct., 1951.

Viscosin is an antibiotic made from *Pseudomonas viscosa*, which in previous tests with bacteria had been found to be active only against mycobacteria. In the present investigation its effect on viruses was studied. Three methods were employed: (1) the contact test, in which mixtures of virus and antibiotic were left at room temperature for 2 hours before injection into embryonated eggs; (2) the embryo protection test, in which the antibiotic was injected one hour before the virus; and (3) the embryo therapeutic test, in which the antibiotic was injected after the virus.

The antibiotic had no apparent effect on the viruses of feline pneumonitis or vaccinia, but was markedly active in protecting the embryos against the virus of infectious bronchitis of chickens and, to a lesser extent, against those of influenza A and B and Newcastle disease of fowls. When employed for the treatment of mice infected with 100 LD50 of influenza A no difference in the death rate resulted from the daily administration of 1 mg. of the antibiotic, but the mice lived about 24 hours longer. *R. Hare*

1162. **Infections with *Pseudomonas aeruginosa* Treated with Polymyxin B**
E. JAWETZ. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 90–98, Jan., 1952. 2 figs., 17 refs.

The widespread and somewhat indiscriminate use of antibiotics is in some hospitals responsible, at least in part, for the establishment of *Pseudomonas aeruginosa* as a secondary invader of burns, wounds, and discharging ears, and also as a cause of urinary-tract infections. In certain circumstances, however, *Ps. aeruginosa* may become the primary infective agent, although it is not a true pathogen. Both types of infection are difficult and stubborn to treat, because the organism has simple nutritional requirements and is readily adaptable to unfavourable environments. While sulphonamide, streptomycin, and aureomycin therapy have occasionally suppressed *Ps. aeruginosa* to an extent sufficient to permit the natural body-defences to gain control of the infection, many strains, however, have been found to be resistant *in vitro* to these drugs.

Polymyxin (A, B, C, D, and E), stable basic polypeptides isolated from *Bacillus polymyxa*, constitute the most active antimicrobial agents against *Ps. aeruginosa*. Earlier studies with polymyxin D revealed its significant degree of nephrotoxicity. The present author has used polymyxin B sulphate (75% purity) for a period of over 2 years in the treatment of 35 selected cases of pseudomonas infections.

Among 28 patients treated for 7 days with daily intramuscular doses of 1·5 to 2·8 mg. per kg. body weight, there was a slight and transient increase in proteinuria

in 7 patients, and a significant increase in the number of leucocytes and epithelial cells in the urine in 3. These changes regressed quickly after the discontinuation of therapy. No other abnormalities were encountered; on the contrary there were 4 instances in which an originally elevated serum creatinine or blood non-protein nitrogen level returned to normal during therapy. As side-effects some neurotoxic symptoms were encountered, such as circumoral and peripheral paraesthesiae, moderate dizziness, and a feeling of weakness; these symptoms disappeared within 24 to 48 hours after discontinuation of the injections.

Many strains of *Ps. aeruginosa* are inhibited *in vitro* by concentrations of 0·1 to 5 μg. per ml. of polymyxin B, and killed by concentrations 2 to 5 times greater.

The topical application of solutions of polymyxin B, 0·5 to 1 mg. per ml., permits the rapid eradication of most strains of this organism without irritation to delicate tissues, mucous membranes, and granulating surfaces, and was used in infections of the middle ear and of the conjunctiva. Absorption of the agent from topical application is negligible. Polymyxin B exerts its most beneficial activity in localized processes on surfaces or within closed systems. *J. W. Czekalowski*

1163. **Terramycin in Epidemic Typhus, Amebic Dysentery and Typhoid**

J. H. KILLOUGH and G. B. MAGILL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1737–1740, Dec. 29, 1951. 2 figs., 7 refs.

This trial of terramycin was carried out in Cairo. Five patients with endemic typhus were treated on the 6th to the 8th day of the disease; 1 case was mild, 3 moderate, and 1 appeared moribund. The dose of terramycin was 75 mg. per kg. body weight per day in 4-hourly doses, following a loading dose of 25 mg. per kg. Treatment was continued until the patient had been afebrile for 2 days; the average dose was about 22 g. during 5 days. Improvement, objective and subjective, began within 24 hours in all patients, and 4 of the patients were afebrile within 3 days. The fifth patient did not become afebrile till the 5th day, and he was mentally confused until the 12th day. In these 5 cases terramycin compared favourably with the reported effects of chloramphenicol and aureomycin.

Seven cases of acute amoebic dysentery were treated. The initial dose was 50 mg. per kg., followed by 150 mg. (in 4-hourly doses) and then 75 mg. per kg. per day for 11 days, totalling about 66 g.; 3 patients complained of anorexia and nausea on the higher dose. The bloody diarrhoea, tenesmus, and other dysenteric symptoms disappeared within 2 to 6 days (average 4 days). Stools and proctoscopic specimens became negative for amoebae after 2 days in 4 patients, and in 4 to 8 days in the other 3. However, the hepatitis, which was present in all cases, disappeared more slowly. In one patient a hepatic abscess developed during treatment with terramycin, but it responded to chloroquine. Thus terramycin alone is not sufficient for the treatment of amoebic dysentery complicated by hepatitis, but its combination with chloroquine (1 g. daily for 2 days followed by 0·5 g. daily for 12 days) will probably cure both phases of the disease. Five of the patients with dysentery were observed for 3 to 5 months, with at least 20 stool examinations. In 2 patients amoebae reappeared and in one of these patients symptoms also returned.

Five cases of typhoid fever were treated after 6 to 11 (average 9) days of illness. All were severe. The dose was 75 to 125 mg. per kg. per day until the patient became afebrile (up to 22 days), total doses ranging from 43 g. in 12 days to 98 g. in 22 days; 3 patients became afebrile in 4½ days (average), but 2 patients gave no response to the treatment; one of these responded quickly when given chloramphenicol, but this patient became a carrier; the others ceased to excrete *Salmonella typhi*. It would appear that terramycin may be effective in some cases of typhoid fever.

F. Hawking

1164. **Anorectal Complications of Aureomycin, Terramycin, and Chloromycetin Therapy**

S. D. MANHEIM. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **51**, 2759–2760, Dec. 1, 1951. 2 refs.

In this paper are reported 100 cases of ano-rectal complications following the administration of aureomycin, terramycin, or chloramphenicol, alone or in combination. The symptom patterns were almost identical. The patients complained of perianal itching associated with pain and with bleeding upon defaecation. These symptoms developed approximately 2 weeks after the ingestion of the drug. In 41 cases diarrhoea also occurred. Proctological examination usually revealed perianal erythema, with thickening and excoriation of perianal skin, and with or without multiple superficial fissures at the anal margins. In a few instances examination also disclosed ulcerative proctitis, ulcerative colitis, or perianal abscess.

The condition was extremely resistant to treatment. Many patients had severe symptoms for as long as 6 to 8 months. Yoghourt or buttermilk appeared to be of benefit in most of the cases in which it was tried.

The author states that the pathogenesis of this anorectal syndrome is as yet undetermined, but that a monilial infection may be responsible.

A. W. H Foxell

1165. **Nisin in Experimental Tuberculosis**

E. M. BAVIN, A. S. BEACH, R. FALCONER, and R. FRIEDMANN. *Lancet* [*Lancet*] **1**, 127–129, Jan. 19, 1952. 7 refs.

It has been suggested that nisin, the antibiotic produced by a strain of *Streptococcus lactis*, might be used in the treatment of infections caused by *Mycobacterium tuberculosis* and other Gram-positive organisms. The present authors, however, found in experiments *in vitro* that although this drug was effective against many Gram-positive organisms, its activity, weight for weight, was less than that of penicillin. Moreover, although nisin was about equivalent to streptomycin in its activity against a human virulent strain of *Myco. tuberculosis in vitro*, its effectiveness against tuberculosis in guinea-pigs was less than would be anticipated from this finding, and it was

very difficult to maintain a level of the antibiotic in the blood which was sufficiently high (approximately 500 units (0·025 mg.) per ml.) to suppress the growth of *Myco. tuberculosis in vitro* without causing toxic effects. The LD50 of nisin for guinea-pigs was about 100 mg. per kg. body weight, when given very slowly intravenously.

The authors conclude that these results indicate that nisin is most unlikely to find a place in therapeutics.

J. W. Czekalowski

1166. **Viomycin and Viomycin with Streptomycin in Streptomycin-resistant Experimental Tuberculosis.** (La viomicina e l'associazione viomicina-streptomicina nella tubercolosi sperimentale da germi streptomicino-resistenti)

A. Masi and P. Moggi. *Rivista di Clinica Pediatrica* [*Riv. Clin. pediat.*] **49**, 853–864, Dec., 1951. 9 figs., 8 refs.

In this study 30 guinea-pigs were inoculated with a standard amount of a culture of tubercle bacilli which was known to be virulent and to be resistant to streptomycin. After 22 days 2 of the animals were killed and the presence of miliary tuberculosis confirmed. The remainder were divided into four groups: untreated controls, those given streptomycin (15 mg. per kg. body weight per day), those given viomycin (36 mg. per kg. per day), and those treated with a combination of the two antibiotics.

At the end of 50 days' treatment the animals were killed and examined and the findings compared. It was evident that viomycin in this dosage was capable of producing favourable results—that is, there was a slower extension of the disease than in control animals or animals treated with streptomycin—but that the combination of viomycin and streptomycin was even more successful. The findings were not sufficient to determine whether or not this was an additive effect of the two antibiotics or a true potentiation; the inference, however, would seem to be that streptomycin need not be abandoned when an infection becomes resistant to it, but that viomycin should be added to the previous regime of treatment.

James D. P. Graham

1167. **Antivital Properties of Ehrlichin, an Antibiotic Produced by *Streptomyces lavendulae***

V. Groupé, J. W. Frankel, M. P. Lechevalier, and S. A. Waksman. *Journal of Immunology* [*J. Immunol.*] **67**, 471–482, Dec., 1951. 21 refs.

Streptomyces lavendulae 3555 produces in the culture medium at least two antiviral substances: the first non-precipitable from culture filtrate at *p*H 2 and active against the Newcastle disease virus; the second acid-precipitable and active *in vitro* against both influenza A and B viruses. This second substance, named "ehrlichin", exerts *in vivo* its inhibitory effect only on influenza B virus; this suppressive action was manifested by a transient inhibition of viral multiplication, embryo survival, and haemagglutinin formation. The suppressive effect of ehrlichin on the formation of viral haemagglutinin was markedly reduced when this substance was injected into the embryonated eggs before, rather than after, their infection with influenza B virus. The authors think that this phenomenon of rapid removal or inactivation of ehrlichin may suggest that this substance affects virus intracellularly—that is, within the host-cell.

In the presence of 3·2% of horse serum ehrlichin is inactive *in vitro* against influenza B virus, but *in vivo* it exerted a minimal but detectable suppressive effect in embryonated eggs and on the degree of pulmonary consolidation in mice.

Crude preparations of ehrlichin are stable to heat and tryptic digestion and are not dialysable; therefore, it should be borne in mind that they may contain a polysaccharide endowed with antiviral properties. Ehrlichin was totally inactive against fungi, bacteria, Chlamydozoaceae, pox viruses, and bacterial viruses.

[This paper contains many useful technical details of methods of testing in embryonated eggs, as well as of the production, concentration, and standardization of the active principle.] *J. W. Czekalowski*

1168. **The Appearance of Allergic Reactions in Treatment with Penicillin and Streptomycin.** (Über das Auftreten allergischer Reaktionen bei der Therapie mit Penicillin und Streptomycin)

R. Schuppli. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **81**, 589–592, June 23, 1951. 4 figs., 2 refs.

In the Basle University Dermatological Clinic 53 cases of cutaneous reaction due to penicillin were observed in the course of 4 years. The most frequent manifestation was urticaria (28 cases, in 17 of which it was generalized, while in 2 it was accompanied by symptoms of serum sickness). Local applications of penicillin may give rise to conjunctivitis, eczema, glossitis, and stomatitis, as well as to congestion of the laryngeal and bronchial mucosa. Intramuscular injections may be followed by the appearance of morbilliform or scarlatiniform eruptions which disappear even if treatment is continued, whereas the urticaria is usually aggravated when treatment is continued and is difficult to cure even after stopping treatment. Dermatophytids, papulo-vesicular eruptions on the palm of the hand containing no fungi, may appear in carriers of fungi. Finally, a combination of various manifestations may occasionally be seen to occur.

These reactions occur within 2 to 20 days of the first contact with penicillin, but more often they appear between the 8th and 14th day. They frequently occur in patients who have never before been treated with penicillin and are consequently not due to sensitization by previous treatment. On the other hand, 35% of the author's patients were suffering from mycoses and, like the mycoses, reactions due to penicillin mainly occur between May and August. Experimentally, guinea-pigs may be sensitized to penicillin and streptomycin by infection with *Trichophyton* or injections of trichophytin. Of 25 patients presenting allergic reactions to penicillin, 90% showed a reaction to trychophytin and 50% to penicillin injected intradermally or subcutaneously, while 5 out of 30 patients with mycoses reacted to intradermal

penicillin. Thus a previous or actually existing mycosis, giving rise to antibodies against penicillin, appears to be the explanation of numerous cases of penicillin sensitivity. Possibly the increased incidence of allergic reactions to penicillin observed at the clinic during 1950 may be attributed to the increased incidence of mycoses due to *Trichophyton rubrum*.

The author suggests that practitioners should avoid using penicillin in the treatment of trifles, and take special precautions in summer, the season of mycoses, and in patients who have previously shown allergic reactions to the antibiotic. A number of cases of eczema due to streptomycin were observed in nurses.

N. Rist (*Excerpta Medica*)

1169. **Clinical and Pharmacologic Studies with Allylmercaptomethyl Penicillin (Penicillin "O")**
C. V. ADAIR, W. G. WOODIN, and P. A. BUNN. *American Journal of Medicine* [*Amer. J. Med.*] **11**, 188–195, Aug., 1951. 1 fig., 15 refs.

In this paper from the Department of Medicine of the State University of New York the substitution of benzyl penicillin by penicillin O in instances of hypersensitivity reaction is discussed, and a series of miscellaneous penicillin-susceptible infections and the reactions of individuals allergic to benzyl penicillin are described. Oral or intramuscular administration of penicillin O to 14 normal individuals gave peak serum levels within an hour, and 200,000 to 500,000 units in water by mouth to healthy fasting adults gave peak serum levels of 0·25 to 1·35 units per ml. in 1 hour, with over 0·03 unit per ml. remaining after 5 hours. Higher levels, of 1·40 to 2·85 units per ml., were obtained with intramuscular doses of 50,000 to 100,000 units. The urinary excretion was equivalent to that of benzyl penicillin in 3 cases, with 33 to 50% of intramuscular and 10% of oral doses recovered within 8 hours. In general, the absorption, distribution, and toxic reactions were equivalent to those of benzyl penicillin.

The 14 cases of miscellaneous infections—which included subacute bacterial endocarditis (α-streptococci), cellulitis of the jaw (*Staphylococcus aureus*), pneumococcal meningitis, pneumonia and bronchopneumonia, and septic sore throat—responded clinically and bacteriologically in a manner similar to that expected for benzyl penicillin.

Some 25 patients, with or without infections, hypersensitive to benzyl penicillin, were given penicillin O as a substitute. In 21 of these the reactions to benzyl penicillin had been actually observed, and notes on 3 cases refer respectively to a serious urticarial rash, a pruritic maculo-papular rash of trunk and limbs, and a generalized pruritic maculo-papular rash. In the majority of patients who had, or developed, a delayed reaction to benzyl penicillin the change to penicillin O was accompanied by a diminution or total disappearance of the allergic phenomena. It was possible to substitute penicillin O for benzyl penicillin with safety in 22 of 25 cases, and to resubstitute benzyl penicillin after 1½ to 14 days without a recurrence of the reaction in 14 out of 15 patients.

Studies of individuals with less common allergic manifestations to benzyl penicillin suggest that penicillin O is not a total substitute, as cross-immune reactions occur. The successful substitution does not indicate desensitization, but suggests that the induced reaction to benzyl penicillin is temporary. If penicillin therapy cannot be discontinued in a patient with a serious infection and a hypersensitivity reaction, then substitution of penicillin O can be considered a safe and beneficial procedure unless there is a history of contact dermatitis.

Malcolm Woodbine

1170. **Allergy to Penicillin O and the Management of Penicillin Sensitivity**
S. SIEGAL. *American Journal of Medicine* [*Amer. J. Med.*] **11**, 196–201, Aug., 1951. 8 refs.

The author, from the Mount Sinai Hospital, New York, refers to previous detailed work (Risman and Boger, *J. Allergy*, 1950, **21**, 425) on benzyl penicillin and penicillins O and BT, in which cross-sensitization was common. He suggests that views as to the usefulness of penicillin O should be modified, as he describes 5 cases illustrating the occurrence of allergy to penicillin O as a result of sensitization to benzyl penicillin. The present paper is not a precise study of the relation of benzyl penicillin to penicillin-O allergy, but is presented as a warning that penicillin O should not be given in cases of benzyl-penicillin sensitivity.

The report is based on the skin testing of patients with a history of penicillin allergy. A simple technique was used, with 20,000 units penicillin per ml. in distilled water; 0·02 of this was injected intradermally for an immediate reaction, the result being read after 15 minutes. This was often negative, but a positive reaction was more commonly obtained after 24 to 48 hours with the delayed skin test, for which 0·10 ml. was given intradermally. A positive reaction consisted of a definite area of erythema 10 mm. or more in diameter, often with indurative oedema.

The details of the 5 cases are then discussed, and it is concluded that it is unsafe to assume that penicillin O can be given safely in place of benzyl penicillin and that preliminary skin tests with the various kinds of penicillin should be performed first—a positive reaction being taken as an indication that treatment should be carried out with caution.

The fundamentals of the management of cases of penicillin hypersensitivity are recapitulated: (1) treatment need not be discontinued for a mild or moderate reaction, and may be continued with symptomatic and anti-allergic remedies (especially in subacute bacterial endocarditis; (2) there is a high tolerance in cases with a history of a single allergic reaction; (3) the skin test has a definite if limited sphere of value: a positive reaction is not equivalent to clinical sensitivity, but implies a greater likelihood of this than a negative reaction, and makes a smaller preliminary dose advisable; (4) if a patient is persistently allergic, then recourse to sulphonamides or the newer antibiotics may be necessary, but desensitization should be seriously considered and those who cannot be desensitized warned against future

exposure; and (5) a desensitization technique requires injections of aqueous crystalline penicillin, in ascending doses, 2 to 3 times a week, starting from 50 to 100 units per ml. and increasing to full therapeutic levels. A conversion from a positive to a negative reaction acts as a useful guide to successful desensitization.

[This paper should be compared with that of Adair, Woodin, and Bunn (Abstract 1169), in which it is claimed that penicillin O is a safe substitute for benzyl penicillin in cases of penicillin sensitivity.]

Malcolm Woodbine

1171. **The Influence of the Dosage Regimen on the Therapeutic Effectiveness of Penicillin G in Experimental Lobar Pneumonia**

L. H. SCHMIDT and A. WALLEY. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **103**, 479–488, Dec., 1951. 22 refs.

In experiments at the Christ Hospital Institute of Medical Research, Cincinnati, Ohio, a "standard" pneumonia was induced in rats by the intratracheal instillation of mucin suspensions of Type 1 pneumococci. Care was taken to ensure that the results obtained in different experiments were reproducible and that an adequate number of rats was used in each experiment. Various total quantities of sodium benzyl penicillin in aqueous solution were given to one group of rats as a single dose and to others at intervals of 2, 4, 8, 12, and 24 hours. By comparing the minimum doses required to secure a 50% recovery rate the authors found that an 8-hourly regimen was the best; it also gave better results than 24-hourly doses of procaine penicillin in another group of rats.

When the surviving rats were killed and examined after 30 days it was found that in a surprising number pneumococci were still harboured in the lungs. The highest proportion was found in rats given procaine penicillin and in those receiving aqueous penicillin at 2- and 4-hourly intervals. Again somewhat surprisingly, the rats which had received the single dose of aqueous penicillin showed the lowest incidence of positive lung cultures.

The rapidity with which bacteriaemia was cleared was also investigated. This experiment suggested that 2-hourly administration was most effective.

Finally, groups of rats were given penicillin in dosages which the first experiment had shown to be effective in producing a 50% recovery rate under the respective schemes of administration, which were used as before—namely, 2-, 4-, 8-, 12-, and 24-hourly doses and a single dose of aqueous penicillin, and 24-hourly doses of procaine penicillin. It was concluded that there was no clear parallelism between the effectiveness of the scheme of dosage and the length of time that bacteriostatic levels were maintained in the plasma. However, there seemed no doubt from the results of all the experiments that 24-hourly administration of procaine penicillin was inferior to repeated administration of an aqueous solution. It is argued that the high efficiency of 8-hourly administration may be related to: (*a*) the susceptibility of surviving pneumococci to phagocytosis; (*b*) the enhanced effect of penicillin against actively growing organisms, which may take some time to reappear after the bactericidal effect of the penicillin dose; and (*c*) that the peaks of high plasma concentration may be advantageous in encouraging the penetration of penicillin in adequate amounts into the tissues.

[It is a pity that such carefully designed experiments cannot be conducted on man. The advisability of applying these results unhesitatingly to man may be questioned, though it is fair to say that the rat and man have a somewhat similar resistance to pneumococcal infections. Nevertheless, they should make clinicians ponder on the efficacy of procaine penicillin given every 24 hours. Clinical impressions are a dangerous guide, but examples could be quoted where treatment became effective only when intermittent aqueous penicillin administration was instituted.] *T. Anderson*

1172. **Further Observations on the Zone Phenomenon in the Bactericidal Action of Penicillin**

H. EAGLE. *Journal of Bacteriology* [*J. Bact.*] **62**, 663–668, Nov., 1951. 4 figs., 8 refs.

In an investigation at the National Microbiological Institute, Bethesda, Maryland, in which one strain each of *Streptococcus faecalis* and Group B *Streptococcus* were used, it was found that the rate of death of these organisms, when exposed to optimal bactericidal concentrations of penicillin, was markedly reduced by subsequent addition of high concentrations of the drug. If the organisms were first exposed to high concentrations of penicillin, and the suspensions then diluted to contain the drug at the lower (optimal) levels, they continued to die at the slow rate of the higher exposure.

The results were considered to show that penicillin exerts at least two qualitatively distinct effects on such "zone-sensitive" strains. Working hypotheses are formulated to explain the observations and are discussed. [Laboratory methods are not given.]

Joyce Wright

1173. **Aureomycin in Experimental Acute Pancreatitis of Dogs**

L. PERSKY, F. B. SCHWEINBURG, S. JACOB, and J. FINE. *Surgery* [*Surgery*] **30**, 652–656, Oct., 1951. 6 refs.

In experiments at the Harvard Medical School aureomycin, given orally for several days before and after the experimental production of acute haemorrhagic pancreatitis in dogs, resulted in 100% survival Only 40% survived if parenteral penicillin or intravenous aureomycin was used. The predominating organisms were found to be clostridia, which had invaded the pancreas from the intestine.

[Bacterial proliferation in dogs does not appear to be identical with that in human beings.]

A. G. Ellerker

1174. **Studies on the Relationship of Tissue Fluid and Blood Levels of Penicillin**

L. WEINSTEIN, G. K. DAIKOS, and T. S. PERRIN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **38**, 712–718, Nov., 1951. 14 refs.

PHYSIOTHERAPY

1175. **Influence of Alternate and Reciprocal Exercise on Work Capacity**
F. A. HELLEBRANDT, S. J. HOUTZ, and R. N. EUBANK. *Archives of Physical Medicine* [*Arch. phys. Med.*] **32**, 766–776, Dec., 1951, 6 figs., 7 refs.

The restoration of functional capacity of the neuromuscular system is dependent on many interrelated variables, such as coordination, rhythm of movements, mobility, strength, endurance, reaction time, and speed of motion. When the first three variables are attained the others usually follow *pari passu*.

With the previous experience of the authors that exercise of homologous parts augments the functional capacity of the weaker side, experiments were devised, at the Medical College of Virginia, to study the influence on work capacity of variation in the method of performing simple repetitive exercise. Alternate and reciprocal wrist-joint extension was carried out against progressively increasing resistance until the requisite number of contractions could no longer be executed at the prescribed rhythm.

Kymograms were made of all ergographic work done. As it was very difficult to evaluate the efficiency of volitional effort without being certain that every contraction made was maximal, all experiments were carried out with the help of highly trained and experienced laboratory assistants.

Normal healthy adults were used and 275 experiments performed. The sum of the work done unilaterally by the two sides was compared with the functional capacity of the same muscle groups when the exercise was done in alternate bouts, reciprocally, or by alternate strokes. The experiments, which lasted from 15 to 30 minutes and required an average of 7 to 9 bouts of 25 repetitive contractions, were repeated at weekly intervals at approximately the same time of the day for any given subject.

From these experiments the authors arrived at the following conclusions: "Change in the way in which a normal range movement is performed repetitively against progressively increasing resistance exercises a significant influence on the functional capacity of the muscle groups involved. All variants of the standard exercise were superior to unilateral performance. Augmentation in work output was greatest when the exercise was performed by alternately contracting homologous muscle groups of the preferred and the non-preferred limb. So-called passive recuperation did not account fully for the change observed. Active recuperation appears to be significantly dynamogenic, whether introduced in the form of alternate strokes, alternate bouts, or reciprocal contraction. It is postulated that the augmentation in functional capacity observed is due to central facilitation and is affected secondarily by spontaneous synergistic cocontractions following a number of clearly defined reflex patterns. How much of the effect is due to psychologic factors incidental to shifts in attention remains yet to be studied." *M. H. L. Desmarais*

1176. **Effectiveness of Different Forms of Heating**
H. M. WHYTE and S. R. READER. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **10**, 449–452, Dec., 1951. 1 fig., 8 refs.

This is a report of an experiment to determine the comparative effectiveness of heating deep subcutaneous tissues by means of long- and short-wave infra-red irradiation, direct contact heaters, and diathermy. The heat generated in the tissues of a number of subjects was measured and recorded by thermocouples on the skin and in the muscles when the lumbar region was heated by these different methods.

It was found that the application of heat by direct contact and of radiant heat from a dark source caused a temperature rise in the skin, but none below a depth of 3 or 4 cm. Short-wave infra-red irradiation was more effective in producing deep heat than the first two methods, but short-wave diathermy could produce deep temperatures exceeding surface temperatures up to a depth of 4 cm. Thus short-wave diathermy is far the most effective method of producing deep heat.

W. Tegner

1177. **Influence of Physical Agents and of Certain Drugs on Intra-articular Temperature**
K. G. WAKIM, A. N. PORTER, and F. H. KRUSEN. *Archives of Physical Medicine* [*Arch. phys. Med.*] **32**, 714–721, Nov., 1951. 6 figs., 6 refs.

The authors, from the Mayo Clinic, review the literature on the effects of various physical agents on intra-articular temperatures. Because of the existence of contradictory reports they decided to study in the trained dog the effects of certain physical agents on the temperatures in the treated and contralateral knee-joints, and compare the simultaneous effects on the subcutaneous and intramuscular temperatures in the treated area.

The physical agents used were: hot packs, short-wave diathermy, microwave diathermy, ice-packs, and percutaneous electric stimulation. In order to determine the influence of vasoconstrictors and vasodilators, adrenaline, vasopressin, nitroglycerin, histamine, and pyrogens were also given singly intravenously.

The authors found that hot packs, short-wave diathermy, and microwave diathermy raised the intra-articular temperature as well as the temperature of the adjacent muscles and subcutaneous tissues. No reflex increase in the temperature of the contralateral knee-joint was noted. Ice-packs had the same effect, but in the opposite direction, and also had no cooling effect on the contralateral joint. Repeated electrical stimulation produced no change in the temperature of the knee-joint, but a slight rise in the subcutaneous and intramuscular temperatures respectively. Intravenous injections of vasoconstrictor and vasodilator drugs produced no significant change in the temperature of the joints and adjacent tissues. Vasopressin, however, produced a gradual but definite reduction in the intra-articular temperature as well as in the intramuscular and subcutaneous temperatures.

M. H. L. Desmarais

Pathology

EXPERIMENTAL PATHOLOGY

1178. **Thromboembolic Pulmonary Arteritis and Vascular Sclerosis. Its Experimental Production in Rabbits by Means of Intravenously Injected Human Amniotic Fluid and Autogenous Blood Clots**
E. E. MUIRHEAD and P. O. MONTGOMERY. *Archives of Pathology* [*Arch. Path., Chicago*] **52**, 505–517, Dec., 1951. 3 figs., 7 refs.

The authors injected amniotic fluid and autogenous blood clots intravenously into two series of rabbits. Considerable acute, subacute, and chronic changes in the walls of smaller branches of the pulmonary arteries followed. The chronic lesions, seen after repeated injections into surviving animals, appeared similar to those seen in " primary " vascular sclerosis of the pulmonary arteries in human patients. Exactly how embolism and thrombosis are connected with the sclerotic changes is not yet known. They may be a cause or part of a common deeper disturbance which is also responsible for pulmonary hypertension. *L. Michaelis*

1179. **Effects of Low Temperatures on Mammary Carcinomas with and without the Mammary Tumor Milk Agent**
L. W. LAW. *Cancer Research* [*Cancer Res.*] **11**, 795–800, Oct., 1951. 3 figs., 23 refs.

In experiments performed at the National Cancer Institute, Bethesda, Maryland, one mammary carcinoma from a mouse of the C3H strain harbouring the mammary-tumour milk agent and 3 mammary tumours from mice of the agent-free C3Hb strain, minced and suspended in 5·3% glucose solution, were frozen and stored at −79° C. for periods varying from 1 to 96 hours. Both freezing and thawing were carried out slowly. After thawing, the tumours were injected subcutaneously and intraperitoneally into C3Hb strain and (R1L×C3Hb) F_1 hybrid mice which served as test animals. The agent-carrying tumour and one of the agent-free tumours were still active after freezing, while the other two tumours without the agent were found to be inactive in both types of test mouse. On transplantation the tumours induced in the hybrid mice with frozen material grew progressively in the (R1L×C3Hb) F_1 hybrids and C3Hb strain mice, but failed to grow in animals of the R1L strain animals.

The assumption of Mann (*Brit. med. J.*, 1949, **2**, 251) that an active agent is liberated from mammary-tumour tissue following freezing is rejected by the author, because of the identical behaviour on freezing of agent-free and agent-carrying tumour tissue. The author concludes that the induction of tumours with frozen material was due to the transfer of living cells. This conclusion is further strengthened by the behaviour on transplantation of the tumours induced in the hybrid mice with frozen material. Had a virus been responsible for the induction of these tumours they would have then had the same genetic constitution as the hybrid mice and would have grown progressively only in these mice. The fact that they grew also in C3Hb mice proves conclusively that the tumours induced with frozen material had the same genetic constitution as the tumour material before freezing, and were therefore induced by cells which survived freezing and storage at −79° C. *L. Dmochowski*

1180. **The Role of Nonspecific Irritation in the Causation of Malignant Change in Tissues.** (Роль неспецифического раздражения в тканевой малигнизации)
A. J. SINAI. *Архив Патологии* [*Arkh. Patol.*] **13**, 32–38, No. 6, 1951. 22 refs.

After a brief review of the Russian literature on the subject, and of articles from British, German, and Italian sources up to 1945, the author describes his own experiments on mice. His idea was to create in the organism of the experimental animal a " general disposition " to the development of a neoplastic process by means of repeated smearing of the scapular region with methylcholanthrene, as a carcinogenic agent, and then to attempt the production of a tumour in a distant region of the skin (abdomen) by means of a non-carcinogenic irritant (croton oil, 2% solution in benzene).

Of 79 animals which survived to the day of the appearance of the first abdominal tumour, 16 developed papillomata on the site of croton-oil application. This incidence is said to have considerably increased later.

The animals were divided into several groups; in some of them methylcholanthrene and croton oil were applied simultaneously, and in others one or the other irritant had been applied before the course of the other was started. Positive results were obtained in all three groups. The number of applications up to the time of the appearance of the first papilloma varied from 7 to 28 weekly doses. Many animals died of malignant tumours at the site of the application of methylcholanthrene before they showed any neoplastic process in the skin of the abdomen. *A. Swan*

1181. **Effects of the Ligation of the Hepatic Artery in Dogs**
D. FRASER, A. M. RAPPAPORT, C. A. VUYLSTEKE, and A. R. COLWELL. *Surgery* [*Surgery*] **30**, 624–641, Oct., 1951. 8 figs., 35 refs.

The authors have studied 31 dogs in which complete ligation of the hepatic artery and its branches had been carried out in the University of Toronto. Of this series 20 received antibiotic therapy, and in this group the operative mortality was reduced from 90% to 35%. The authors consider that death in these cases is due to a centrilobular ischaemic necrosis on which bacterial proliferation may or may not be superimposed. Impairment of liver function occurred in more than half the surviving

animals, but this was only transitory. Penicillin therapy appeared to be as effective in promoting survival as a wider range of antibiotics. *A. G. Ellerker*

1182. **Partial Hepatectomy in the Dog. An Experimental Study**
M. S. DeWeese and C. Lewis. *Surgery* [*Surgery*] **30**, 642–651, Oct., 1951. 3 figs., 24 refs.

Permanent ligation of the branch of the portal vein supplying two of the three primary lobes of the liver and simultaneous temporary occlusion of the common hepatic artery are compatible with life in the dog and permit a relatively bloodless operative approach to the liver. Such a procedure has not produced clinically significant physiologic disturbances in dogs studied as long as 6 months post-operatively. Maintenance of uninterrupted portal blood flow through a relatively small segment of the liver materially reduces the risk of central occlusion of the remainder of the hepatic blood supply during partial hepatectomy in the dog.—[Authors' summary.]

1183. **Hepatic Necrosis Induced by Dietary Means—3. The Effect of Various Dietary Modifications on the Liver Lipid Fractions and on the Development of Necrosis**
M. R. Abell and J. M. R. Beveridge. *Archives of Pathology* [*Arch. Path., Chicago*] **52**, 423–427, Nov., 1951.

The authors previously showed by chemical and histological studies that certain changes in liver lipids occurred before and during the development of necrosis in rats living on a basal necrogenic diet low in the sulphur-containing amino-acids and in α-tocopherol. The present paper describes experiments designed to determine whether those changes were constant features of the development of the hepatic lesions.

Groups of 20 young male Sprague-Dawley rats, of weights ranging from 101 to 155 g., were fed on a necrogenic diet of the following composition: Fleischmann's active dried baker's yeast, 18%; corn starch, 71%; lard, 5%; a salt mixture, 3%; cod-liver oil, 2%; and a sugar and vitamin mixture, 1%. This last supplied the following amounts of vitamins of the B complex in every 8 g. of food: aneurin, 0·02 mg.; riboflavin, 0·025 mg.; pyridoxine hydrochloride, 0·02 mg.; and calcium pantothenate, 0·1 mg.

Equivalent amounts of starch were replaced in various groups of animals by supplements as follows: Group 1, 2 mg. α-tocopherol (dissolved in ethyl laurate) daily by mouth; Group 2, 0·5% L-cystine; Group 3, 0·625% choline chloride; Group 4, crystalline vitamins A (acetate) and D (calciferol) at levels of 1·38 mg. and 0·02 mg. respectively per 100 g. of diet, these levels contributing approximately the same numbers of units of vitamins A and D as did the 2% level of cod-liver oil incorporated into the basal diet. The cod-liver oil was replaced by an equal amount of lard. Group 5, 5 mg. α-tocopherol quinone (dissolved in ethyl laurate) daily by mouth.

Chemical and histological examination of the liver was made after 104 to 106 days. The results demonstrated that fatty infiltration occurred during the pre-necrotic period; choline chloride only partly prevented this accumulation of fat. The levels of free cholesterol remained constant until necrosis appeared, when they rose considerably. The cholesterol ester fraction increased in the pre-necrotic period and further at the time of development of necrosis. The change in free and esterified cholesterol at the time of necrosis thus occurred in all groups. The authors conclude that these changes are " inevitable accompaniments of the process ".
B. G. Maegraith

1184. **Studies on Hepatic Necrosis Induced by Dietary Means—4. Conditions Affecting the Production and Prevention of Massive Liver Necrosis**
M. R. Abell and J. M. R. Beveridge. *Archives of Pathology* [*Arch. Path., Chicago*] **52**, 428–440, Nov., 1951. Bibliography.

In an attempt to elucidate further the factors involved in the production of massive liver necrosis in rats fed diets low in methionine, cystine and α-tocopherol, experimental conditions have been varied with regard to initial weight and sex of the test animal and with regard to various dietary supplements. The greater the initial weight of the rats, the longer the time required for liver necrosis to develop. Female rats were found to be definitely more resistant to hepatic damage than males. The inclusion of cod-liver oil greatly increased the necrogenic quality of the basal diet.

Of the lipotropic and antilipotropic substances tested, choline, inositol, cholesterol, and cystine, only the last had any effect on the development of liver necrosis. This substance displayed its well-known prophylactic action. In confirmation of previous reports, α-tocopherol, like cystine, prevented the development of hepatic damage. α-Tocopherol quinone did not act as a structural antagonist to α-tocopherol in the development of liver necrosis, and indeed it actually caused a diminution in the necrogenicity of the basal diet. A similar but definite effect was noted for synthetic vitamin K (menadione). None of the purines, uric acid, theophylline, or xanthine had any prophylactic action. A tyrosine supplement (1%) had no demonstrable effect, but the addition of ascorbic acid (0·625%) decreased slightly the necrogenicity of the basal diet.

Heat inactivation of active baker's yeast did not alter the effect of the basal diet, but substitution of brewer's yeast for the baker's yeast caused a decrease in its necrogenicity. Supplementation with desiccated thyroid (0·3%) greatly increased the necrogenic property of the basal diet, causing death from hepatic necrosis in half the normal time. The antithyroid drug, propylthiouracil, on the other hand, appeared to prevent liver necrosis, although the animals died of other causes after an interval on the test diet greater than that required to induce necrosis in rats on the basal diet. Sulfaguanidine and aureomycin both caused definite amelioration of the necrogenic property of the basal diet.

With the exception of vitamin B_{12} alterations in the vitamin supplement had no effect. In the case of B_{12} there appeared to be a slight increase in the time required for death due to liver necrosis, but this difference could

not be shown to be of statistical significance. The implications of some of these results are discussed.—[Authors' summary.]

1185. **Microscopic Observations of the Living Mammalian Kidney: the Effect of Crush Injuries, Shock, and Adrenalin on the Cortical Blood Flow**
J. F. R. Fleming and W. G. Bigelow. *Surgery* [*Surgery*] **30**, 994–1003, Dec., 1951. 3 figs., 18 refs.

The authors, at the University of Toronto, observed the cortex of the rabbit's kidney by direct microscopy in the living animal, for which they used a transillumination technique. An attempt to produce the crush syndrome was made by pounding the legs. Changes in urea clearance and blood urea concentration, together with other observations, showed that a renal change occurred after this procedure, but the full picture of crush syndrome did not develop. For 24 to 48 hours after the procedure cortical blood flow slowed markedly, but did not cease, and agglutination of erythrocytes into clumps was apparent. These clumps could be seen to obstruct the vessels intermittently, and it is suggested that this blockage plays a part in the genesis of crush syndrome.
G. M. Bull

1186. **The Effect of Acidosis and Alkalosis on the Plasma Potassium Concentration and the Electrocardiogram of Normal and Potassium Depleted Dogs**
W. B. Abrams, D. W. Lewis, and S. Bellet. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **222**, 506–515, Nov., 1951. 5 figs., 39 refs.

1187. **The Therapeutic Activity of Xanthopterin and *para*-Aminobenzoylglutamic Acid in Experimental Macrocytic Anaemia in the Rat.** (Attivita terapeuticà della associazione xantopterina-acido *p*-aminobenzoilglutamico nella anemia macrocitica sperimentale del ratto)
L. Tentori and G. Vivaldi. *Rendiconti Istituto Superiore di Sanità* [*R.C. Ist. sup. San.*] **14**, 768–778, 1951. 4 figs., 4 refs.

Following their previous work on the action of folic acid on the anaemia produced in rats on a folic-acid-deficient diet, the authors have studied the effects of the two parts of the folic acid molecule—xanthopterin and *p*-aminobenzoylglutamic acid.

The rats were kept on a diet deficient in folic acid, to which streptomycin (1 in 1,000) had been added, for about 180 days, during which time anaemia developed. The animals were then divided into 4 groups. Group 1 received folic acid in a dose of 200 μg. weekly, and showed a rise in erythrocyte count with a reticulocyte peak. Group 2, which received *p*-aminobenzoylglutamic acid, 300 μg. weekly, showed no response. Xanthopterin in a dose of 200 μg. weekly was given to Group 3, and produced a slight rise in erythrocyte count, which the authors regard as a non-specific effect. Group 4 received weekly *p*-aminobenzoylglutamic acid 300 μg. and xanthopterin 200 μg. simultaneously, and showed a response equivalent to that obtained with folic acid in Group 1. The authors suggest that the complete folic acid molecule is necessary for erythropoietic response, and that rats can synthesize it from the constituent parts of the molecule if these are supplied.
R. F. Jennison

1188. **Changes in the Argyrophil Granularity of the Tissues of the Brain and Nerve Roots, Arterial, Cardiac, and Striated Muscle, and the Liver in Dogs Subjected to Neuromuscular Training (Running) and to Excessive Exercise.** (Об изменении аргирофильной зернистости в мозговой ткани, в нервных корешках, в артериях, в сердечной и в других поперечнополосатых мышцах, в печени у собак, подвергнутых нервно-мышечной тренировке (в беге) и перенапряжению)
P. E. Snesarev. *Архив Патологии* [*Arkh. Patol.*] **13**, 40–51, No. 6, 1951. 13 figs., 9 refs.

Using his own modifications of silver stains for the demonstration of argyrophilic fibres and argyrophilic granules, the author studied various tissues of normal dogs and of 2 dogs subjected to excessive exercise to the point of exhaustion.

Argyrophil granules were found not only in the tissues of the nervous system, but also in "purely mesenchymal tissues" (in the muscle fibres, nerve sheaths, and the connective tissue in general). It appears that under the influence of excessive exercise large-sized granules are formed in the nerve cells, muscle cells, and many other types of cell. The argyrophil fibres have not been observed to undergo any consistent changes. These large granules are said to be quite distinct from smaller mitochondrial granules. A relationship between the argyrophilic fibres and large granules is suspected, but not clarified.

The article is illustrated by 13 photomicrographs.
A. Swan

1189. **Studies on the "Alkaline" Phosphatase Associated with Regenerating Connective Tissue Fibers**
B. S. Gould and N. I. Gold. *Archives of Pathology* [*Arch. Path., Chicago*] **52**, 413–422, Nov., 1951. 4 figs., 23 refs.

In experiments at the Massachusetts Institute of Technology the serum alkaline-phosphatase level in rats was raised to 193 to 440 units by high-fat diets and lowered to 12 to 22 units by starvation (normal range, 47 to 92 units). Small circles of skin were removed on each side, and the healing areas excised after 2, 7, or 9 days and stained for collagen fibres and alkaline-phosphatase activity. All animals, irrespective of serum phosphatase level, showed no true collagen fibres and no phosphatase activity in the 2-day wounds, but abundant young connective tissue and marked phosphatase activity in the 7- and 9-day wounds. In rats in which phosphatase inhibitors (cysteine or thioglycolate) were injected into the healing skin wounds three times daily for 8 days, the tissue phosphatase activity was low, but the degree of fibrogenesis was the same as in normal controls.

Scorbutic guinea-pigs, which have a low serum alkaline-phosphatase level (less than 3·3 units), showed no fibre formation and almost no alkaline-phosphatase activity

in a 14-day wound. Application twice daily of a powerful preparation of calf intestinal phosphatase in a sodium alginate base made no difference to the degree of fibre formation or tissue phosphatase activity.

M. Lubran

CHEMICAL PATHOLOGY

1190. **Observations on Erythrocyte and Plasma Cholinesterase Activity in Dyscrasias of the Blood**
H. H. SCUDAMORE, L. J. VORHAUS, and R. M. KARK. *Blood* [*Blood*] **6**, 1260–1273, Dec., 1951. 7 figs., 26 refs.

The authors have analysed the level of cholinesterase present in erythrocytes and plasma in various blood dyscrasias and in healthy individuals. Erythrocyte cholinesterase activity was found to be low in patients with pernicious or hypoplastic anaemia, and high in patients with anaemia secondary to haemorrhage or in other types of anaemia in early remission. The plasma cholinesterase activity usually reflected the general clinical status of the patients and was in general related to the albumin concentration of the serum. It improved only slowly during remission and did not show any marked rise, as did that of the erythrocytes, at the time of the reticulocyte response. The authors suggest that erythrocyte cholinesterase activity may be related to erythropoiesis and reticulocytosis. Normal erythrocyte cholinesterase activity is present when there is a balance between the numbers of young and mature erythrocytes in the peripheral blood. *Janet Vaughan*

1191. **Plasma Antithrombin Patterns in Disturbances of the Pancreas**
I. INNERFIELD, A. ANGRIST, and J. W. BENJAMIN. *Gastroenterology* [*Gastroenterology*] **19**, 843–854, Dec., 1951. 5 figs., 14 refs.

In this study from the New York Medical College the authors describe a test for plasma antithrombin which was found useful in the diagnosis of diseases of the pancreas. A modification of Quick's method was employed in which the patient's plasma was defibrinated by standard thrombin and incubated with further standardized thrombin. At intervals this was added to normal plasma, and clotting times were read in conjunction with a control series. A positive result was recorded when the clotting time was not less than 300 seconds after 15 minutes' incubation, and at least 100% greater than normal after 5 minutes' incubation.

The test was found to give an accurate measure of the plasma antithrombin level, and a high level was found in 50 out of 55 cases of acute pancreatitis. These "positive test" results are attributed to an increased blood trypsin content raising the antithrombin level. Occasional false positive results were found in cases of "acute abdomen", which included 3 cases of acute cholecystitis and one case of perforated peptic ulcer. However, in 97·1% of 304 cases of acute abdominal emergency (excluding pancreatitis) the test was negative.

A depressed antithrombin titre was seen in 1 out of 13 cases of fibrocystic disease of the pancreas, 9 cases giving a "low normal" test result. This was attributed to the effect of decreased trypsin formation and consequent low plasma antithrombin levels. Of 5 cases of carcinoma of the body of the pancreas, in 2 the plasma antithrombin level was low: this may be a cause of the occasional occurrence of thrombo-embolic phenomena in that condition.

[It would seem that the antithrombin test may be valuable in differentiating acute pancreatitis from other acute abdominal emergencies. Reference to the original is necessary for the detailed technical steps in the test.]

I. McLean-Baird

1192. **Serum Enzymatic Response (Diastase and Lipase) after Stimulation of External Pancreatic Secretion with Secretin and Methacholine. A Preliminary Report**
R. SANCHEZ-UBEDA and L. M. ROUSSELOT. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **93**, 283–291, Sept., 1951. 2 figs., 44 refs.

This article describes work carried out to determine the pattern of response of serum diastase and lipase following administration of methacholine and secretin as pancreatic stimulants.

There is some evidence to show that the normal pancreas produces a constant response which is considerably less than the values found in cases of chronic pancreatitis and perhaps even of carcinoma. It is suggested that eventually, after further study, some test of this nature might help in the diagnosis of pancreatic lesions. *J. Marshall Pullan*

1193. **Preliminary Clinical Observations of Serum Lipase Activity as Determined by a Colorimetric Method**
A. M. SELIGMAN, P. GLOTZER, and L. PERSKY. *Surgery* [*Surgery*] **30**, 923–930, Dec., 1951. 17 refs.

1194. **Observations on Some Liver Function Tests in Infancy**
S. D. V. WELLER. *Great Ormond Street Journal* [*Gt Ormond Str. J.*] No. 1, 26–31, June, 1951. 3 refs.

Liver function tests were performed on 53 children under 1 year of age and suffering from the following liver disorders: anatomical obstructive jaundice (19), obstructive jaundice from rhesus incompatibility (3), obstructive jaundice of uncertain origin (2), congenital hepatitis (5), prolonged neonatal jaundice (9), cirrhosis (5), liver failure with gastro-enteritis (4), and miscellaneous disorders (6). The tests carried out were the Takata–Ara, thymol turbidity, serum alkaline-phosphatase, and van den Bergh tests.

The Takata–Ara test seldom gave positive results, and these were misleading, especially in the age group under 3 months. The thymol turbidity test was little better. "In general, with increasing liver damage, both Takata–Ara and thymol turbidity reactions were likely to become abnormal, but this often fails to occur, and one of our cases shows that the reverse can happen, with the tests improving in spite of liver damage becoming worse." When cord blood from normal infants was tested negative results were obtained.

The serum alkaline-phosphatase reaction, on the other hand, was abnormal in 80% of cases. The test shed no useful light on the nature of the causative illness, and it is noteworthy that intrahepatic disease gave slightly higher readings than extrahepatic obstruction. In liver failure from gastro-enteritis the phosphatase level was lower than with other disorders.

The van den Bergh test and serum bilirubin level were not helpful in distinguishing the cause of liver disease. It was noted that the bilirubin level in total biliary atresia often remained unexpectedly low.

" It would appear from the above results that these tests in the first year of life are no reliable help to the clinician." *M. MacGregor*

MORBID CYTOLOGY

1195. **The Pathogenesis of Inclusion Bodies.** (Beitrag zur Pathogenese der Einschlusskörper)
H. U. ZOLLINGER. *Schweizerische Zeitschrift für Allgemeine Pathologie und Bakteriologie* [*Schweiz. Z. allg. Path.*] **14**, 446–455, 1951. 12 figs., 33 refs.

The formation of inclusion bodies inside cell nuclei is the result of a disturbance of intracellular protein metabolism. This may be brought about by viruses, or by physical and chemical agents which inhibit mitosis, such as lead, aluminium, and ionizing radiations. Inclusion bodies also occur in the absence of a recognizable cause. Their presence in malignant cells is associated with pathological growth stimulation, although the possibility of virus action cannot altogether be excluded in the case of mammary tumours of mice which have been induced by the " milk factor ". Inclusion bodies are therefore to be regarded as " pathologically changed nucleoli ", and are by no means specific of virus diseases.

R. J. Ludford

1196. **Cytological Study of the Upper Gastro-intestinal Sediment. Its Value, as Correlated with Roentgenologic and Clinical Findings, in the Diagnosis of Cancer**
J. E. IMBRIGLIA, G. N. STEIN, and M. S. LOPUSNIAK. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 120–122, Sept. 8, 1951. 7 refs.

Working at the Graduate Hospital of the University of Pennsylvania the authors have compared the diagnosis of cancer of the oesophagus and stomach by histological examination of the cells of the gastric sediment with the radiological diagnosis, and have correlated their findings with the clinical, surgical, and post-mortem diagnosis. Full details of the technique of collection and staining are given.

Of 13 patients with lesions of the oesophagus, 8 had carcinoma; this was correctly diagnosed by cytological examination in 7 of them, while all 8 were correctly diagnosed radiologically. Of 12 cases of lesions of the cardia of the stomach, 2 were malignant, and 1 was correctly diagnosed cytologically and 1 radiologically. Of the 10 benign lesions only 1 was incorrectly diagnosed cytologically as malignant, though radiologically 2 were diagnosed as malignant and 4 as equivocal. Of 35 lesions of the body of the stomach, 17 were malignant, and 15 of these were correctly diagnosed cytologically, while 2 were diagnosed as benign, but these 2 were intramural carcinomata without ulceration or malignant change in the gastric epithelium. One intramural carcinoma was incorrectly diagnosed radiologically, all the other cases of carcinoma being correctly diagnosed. Of the 18 benign lesions, 1 was incorrectly diagnosed cytologically as malignant, while 5 were so diagnosed radiologically and 2 more as equivocal. Of 13 lesions in the antrum of the stomach, 4 were malignant and all of these were correctly diagnosed cytologically, while 3 were correctly diagnosed radiologically and 1 was diagnosed as equivocal. Of the 9 benign lesions, 2 were diagnosed as malignant cytologically, while radiologically 1 was classed as malignant and 2 equivocal. All 12 lesions of the pyloric canal were benign and one of these was incorrectly classed as malignant cytologically; radiologically, 8 were correctly diagnosed, 2 as malignant and 2 as equivocal. The radiographs were reported on by residents in training.

Walter H. H. Merivale

1197. **Morphology of the Malignant Squamous Cell. A Study of Six Thousand Cells Derived from Squamous Cell Carcinomas of the Uterine Cervix**
J. W. REAGAN and R. D. MOORE. *American Journal of Pathology* [*Amer. J. Path.*] **28**, 105–127, Jan.–Feb., 1952. 19 figs., 31 refs.

The authors examined a minimum of 100 malignant-looking cells from each of 60 confirmed cases of squamous-cell carcinoma of the uterine cervix. They evaluated the various changes observed according to the relative frequency of their occurrence in malignant cells as compared with cells from cases of non-malignant disease. The most significant changes were: diffusely granular nuclear chromatin, altered nuclear–cytoplasmic ratio (especially if greater than 1 : 2), nuclear hyperchromatism, irregularity of nuclear size and shape, and the presence of a macronucleolus. The authors believe, however, that the significance of the last three has been overstressed. A cell should possess at least two of these characteristics before it can be identified as a malignant-tumour cell. The evaluation of smears must take into account all the criteria, and " should be based on the specimen in general rather than on an isolated cell ".

C. V. Harrison

1198. **The Prostatic Smear and its Clinical Usefulness**
H. PETERS. *Journal of Urology* [*J. Urol.*] **66**, 770–777, Dec., 1951. 8 figs., 9 refs.

Cytological examination of the prostatic secretion is becoming increasingly important. The normal prostatic secretion contains only a few cells, but there are many cells in the secretion from patients with benign prostatic hypertrophy—columnar cells, superficial squamous cells, and a varying number of leucocytes. In the presence of prostatitis there are usually many desquamated cells and inflammatory cells. Opinion is divided about the useful-

ness of cytological examination in carcinoma of the prostate. There are sometimes large sheets of malignant cells in the smear, and the clinical diagnosis can often be confirmed in this way. The prostatic smear may change after oestrogen therapy; the cells are no longer so obviously malignant, and in some cases the altered malignant cells disappear altogether from the secretion. It is probable that in all patients receiving oestrogen therapy for carcinoma of the prostate regular cytological examinations of the prostatic fluid should be carried out.

Victor W. Dix

MORBID ANATOMY AND HISTOLOGY

1199. **The Adrenal Cortex in Rheumatic Disease. Pathologic Study with Special Reference to Effects of Cortisone and Corticotropin**

L. Sokoloff, J. T. Sharp, and E. H. Kaufman. *Archives of Internal Medicine* [*Arch. intern. Med.*] **88**, 627–639, Nov., 1951. 6 figs., 25 refs.

The weight, cholesterol content, morphology, and zonal thickness of the adrenal glands were determined in 126 patients examined post mortem, including otherwise healthy children and adults who died suddenly as the result of trauma (15 cases), patients with pituitary disease (3 cases), those given corticotrophin or cortisone (33 cases), and 65 others with various diseases.

The mean weight range of the adrenal glands of adults with endocrine disease was higher than that of the healthy subjects (6·3 to 18·4 g., with a mean of 11 g., compared with 6·1 to 13·5 g. and a mean of 9·3 g.); a linear correlation was found between adrenal weight and mean cortical thickness (obtained from 40 thickness measurements in each case, made on tracings of a magnified projection).

Cholesterol content ranged between 4·7 and 14·9 g. per 100 g. wet weight (mean 9·6 g. per 100 g.) in healthy adults as compared with a somewhat decreased amount in diseased patients (0·5 to 11·3 g. per 100 g.; mean 5 g. per 100 g.).

In 3 cases with pituitary tumour the cortex was thinner and the gland smaller, and the cholesterol content was low. Increase in thickness was due to widening of the zona fasciculata, but there was little specific difference between diseases, nor were glands from cases of disseminated lupus erythematosus, rheumatic fever, and rheumatoid arthritis different from those in cases of other diseases, whether the patient had or had not been given hormone therapy. The adrenals of 2 patients who died while on massive corticotrophin therapy (over 2 g.) showed a great increase in weight (to 28 g.), with hyperplasia and hypertrophy affecting all zones. In patients who died 9 days or more after the discontinuance of corticotrophin therapy the glands appeared no different from those of patients who had not been given such therapy, nor were specific changes seen in patients who had received less than 2 g. of either hormone. The adrenals of some of the patients who had received large amounts of cortisone showed atrophy, but there was no atrophy in a patient receiving 5·2 g. in 18 days. Patients who died 19 days or more after cessation of a long and intensive course of cortisone therapy showed no atrophy or morphological change.

E. G. L. Bywaters

1200. **Pulmonary Fibrosis Secondary to Pneumonia**

S. H. Auerbach, O. M. Mims, and E. W. Goodpasture. *American Journal of Pathology* [*Amer. J. Path.*] **28**, 69–87, Jan.–Feb., 1952. 9 figs., 27 refs.

In 12% of 307 consecutive necropsies performed between 1946 and 1950 pulmonary fibrosis secondary to pneumonia was found, including organized alveolar exudates, alveolar-wall fibrosis, and organized uraemic exudates. The amount of fibrosis varied from obvious areas of carnification to foci found only on microscopical examination. In a control series of 100 cases from each of the years 1940 and 1930 the incidence of similar fibrosis was lower, being 7% and 5% respectively. The authors believe this higher incidence is related to antibacterial therapy, and that some cases are due to viral pneumonia.

C. V. Harrison

1201. **Myxoedema: an Autopsy Report with Histochemical Observations on the Nature of the Mucoid Infiltrations**

D. B. Brewer. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **63**, 503–512, July, 1951. 8 figs., 39 refs.

Since the introduction of thyroid treatment by Murray in 1891 very few reports of necropsies on untreated cases of myxoedema have been published, and consequently there are many unanswered problems concerning the disease. The present study, carried out at the University of Birmingham, was directed particularly to elucidating the nature of the so-called mucoid infiltrations and the changes in the myocardium in an advanced case of myxoedema in a man of 56 who died after one day's thyroid treatment. Histochemical studies were made of the mucoid infiltrations of the skin, tongue, and myocardium. It was concluded that the material infiltrating the tongue was probably a mixture of mucoproteins containing hyaluronic acid and chondroitin sulphuric acid, whereas that infiltrating the myocardium consisted of a histochemically distinct mucoprotein. The swelling in ordinary oedema differs from that observed in advanced myxoedema: as shown by Byrom (*Clin. Sci.*, 1933–34, **1**, 273), there is an increase in extracellular fluid, which contains an abnormal accumulation of protein, and the swollen and apparently oedematous tissue retains its fluid even when cut up into small pieces. According to the present author it seems probable that the abnormal extracellular protein is conjugated with hyaluronic acid and chondroitin sulphuric acid or some other strongly acid mucopolysaccharide. Such conjugates form hydrophilic suspensoids and are able to attract water very strongly, the water becoming firmly bound to the hydrophilic groups in the molecule. If the suspensoid is in the form of a gel, this mechanism would account for the increase in interstitial fluid and for the firm, non-pitting nature of the swelling. When the mucoprotein is broken down under the influence of thyroxine, the interstitial fluid is freed, a rapid diuresis results, and the swellings disappear.

Various histological changes have been described in the " myxoedema heart ", such as myocardial fibrosis, vacuolation of the muscle fibres, interstitial oedema, and other unspecified nuclear and cytoplasmatic changes. Several authors, however, have described basophilic mucoid infiltration of the striated and non-striated muscle fibres and of the myocardium such as was found in the case now reported, and the present author considers that whereas the presence of a few areas of basophilic degeneration is of no significance, the great increase in their numbers constitutes the histological characteristic of the " myxoedema heart ". *E. Forrai*

1202. **A Biopsy Study of Chronic Gastritis and Gastric Atrophy**

R. MOTTERAM. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **63**, 389–394, July, 1951. 12 figs., 10 refs.

In this paper from the Walter and Eliza Hall Institute of Medical Research and the Royal Melbourne Hospital, Australia, the author reports the results of biopsy of the gastric mucosa by means of a flexible tube as described by Wood (*Lancet*, 1949, **1**, 18). The depth of insertion of the tube was controlled so that the site of the biopsy was in the body of the stomach, and specimens were usually obtained from two different levels to render the sampling more representative of the general state of the body mucosa. The routine stains used were haematoxylin and eosin, haematoxylin and Mayer's mucicarmine, and a composite trichrome stain which gave good differential staining of chief and parietal cells.

The procedure was carried out on 150 patients complaining of a variety of dyspeptic symptoms and in whom opaque-meal radiography showed no gross abnormality, and on 43 patients with pernicious anaemia. No significant change was seen in the gastric mucosa of 55 of the cases of dyspepsia. In the remainder various degrees of atrophy of chief and parietal cells were present, and 2 types of lesion could be recognized: (1) superficial gastritis with minimal atrophy (45 cases); and (2) gastritis extending into the depths of the mucosa with moderate to severe atrophy (50 cases).

In the 43 cases of pernicious anaemia there was almost complete atrophy of chief and parietal cells, but gastritis was absent. There was close correlation between the degree of atrophy present and the functional defect as observed in the histamine test meal. This atrophy, combined with intestinal metaplasia and absence of wandering-cell infiltration, made up a pattern distinctive of this disease. Adequate liver therapy failed to alter the mucosal appearances. Half of the patients had received treatment for several years and yet the gastric mucosa showed no sign of a return to the normal pattern.

Apart from alcohol in some cases, no aetiological factor in the production of gastritis was known. Mucosa from patients with superficial gastritis due to excess of alcohol returned to normal after withdrawal of the alcohol. Biopsy was performed in 20 cases of chronic alcoholism with associated malnutrition and enlarged fatty liver which, in some cases, had progressed to portal cirrhosis. After 2 weeks' stay in hospital the gastric mucosa was normal in 19. This was contrary to the suggestion of Faber that minor grades of recurring damage result in chronic atrophic gastritis.

E. Forrai

1203. **Vascular Patterns in the Cirrhotic Liver**

J. B. WILSON. *Edinburgh Medical Journal* [*Edinb. med. J.*] **58**, 537–547, Nov., 1951. 6 figs., 19 refs.

The vascular patterns of 3 normal and 6 cirrhotic livers obtained from the Pathology Department of the Royal Infirmary, Edinburgh, were examined after injection of neoprene latex by Trueta's method. In various specimens injections of latex were made at a high pressure into the hepatic artery, the portal vein, and the hepatic vein. Tissue was dissolved by immersion in strong hydrochloric acid. Sample blocks of tissue were removed at the time of injection and embedded in celloidin for histological examination.

Considerable variations in vascular pattern were observed in both normal and cirrhotic livers. Among the latter some showed dissociation of hepatic arterial and portal venous trees; in others the normal relationship was preserved. In severe cirrhosis the hepatic arterial tree appeared to predominate over the portal venous tree—the reverse of normal Regenerated nodules of liver tissue in 2 cases appeared to lack blood supply; in 2 others these nodules were supplied mainly by the artery. No " unduly early communication " of portal vein and hepatic artery was demonstrated in the cirrhotic livers.

[The high pressures used for the injection of latex (for example, 200 mm. mercury) into the hepatic and portal venous systems make the results difficult to interpret. Injection of Hycar latex at a much lower pressure (for example, 20 mm. mercury) produces a completely different picture in the normal liver (Andrews *et al.*, *Ann. trop. Med. Parasit.*, 1949, **32**, 229). At a low pressure there is no difficulty whatever in penetrating the portal venous tree, so that the vessels are filled all over the surface and throughout the substance of the organ. The author's statement that in a normal liver " the injection of the hepatic vein appeared all over the surface of the liver, while injection of the portal vein appeared there only occasionally—further argument that the unit of the liver is the portal vein surrounded by central veins "—is more of a comment on the limitations of the technique he used than on the structure of the liver. This work should be repeated with less viscous latex capable of being injected at more nearly physiological pressures.] *B. G. Maegraith*

1204. **The Kidney of Scleroderma**

H. C. MOORE and H. L. SHEEHAN. *Lancet* [*Lancet*] **1**, 68–70, Jan. 12, 1952. 3 figs., 10 refs.

In 3 cases of scleroderma in which death was due to renal failure 2 distinctive lesions were found in the vessels of the kidney. The first of these consisted in a concentric, mucoid, intimal thickening of the proximal parts of the intralobular arteries, while the second was characterized by fibrinoid necrosis in the terminal parts of these arteries and in the afferent arterioles. The consequent ischaemic changes in the cortex were presumably responsible for the renal insufficiency.

R. Heptinstall

Bacteriology

1205. **Laboratory-acquired Infections**
S. E. SULKIN and R. M. PIKE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1740–1745, Dec. 29, 1951. 1 fig.

This paper presents a survey of 1,342 cases of infection (with 39 fatalities) presumably acquired in laboratories in the U.S.A. during the last two decades. Of these infections, 775 were bacterial (with 19 deaths), 200 were rickettsial (12 deaths), 39 due to parasites, and 63 to fungus (2 deaths). Brucellosis, tuberculosis, tularaemia, typhoid fever, and streptococcal infections accounted for 31% of all infections, and for 72% of bacterial infections. The highest fatality rate (4·5%) was caused by virus diseases.

Most cases (1,010) occurred among trained scientific workers; only 63 cases were in students. To find the total laboratory personnel, questionaries were sent out to most laboratories in the U.S.A., and from their returns the population at risk over the last 20 years was calculated to be about 121,000. From this, the attack rate for various types of institutions and of personnel was worked out. Research institutions had the highest attack rate at 4·1 per 1,000 workers. Public health laboratories were next with only 0·7 per 1,000. Among trained scientific workers the rate was 1 per 1,000, this being more than twice that of any other group. The source of infection could not always be accurately traced, but in most cases it could be shown that the victim had worked with the agent involved. At least 173 infections were by air-borne transmission; 215 infections were from known accidents; and 98 infections were contracted in the performance of post-mortem examinations.

Attention is drawn to aerosolization of infective agents as an unrecognized hazard. Various types of safety measure are described in detail. Immunization seems not necessarily to prevent infection, although it lessens the severity of the disease. Chemotherapeutic agents are recommended, but must be given promptly.

Jessie Freeman

VIRUSES

1206. **The Growth Curve of the Lansing Strain of Poliomyelitis Virus in the Central Nervous System of the Mouse**
J. D. AINSLIE. *Journal of Experimental Medicine* [*J. exp. Med.*] **95**, 1–7, Jan. 1, 1952. 3 figs., 8 refs.

In 7 experiments carried out at the University of Michigan the virus content was determined in the brains and cords of mice killed at intervals after intracerebral inoculation of 10% suspensions of brain containing approximately 2,000 LD50 of the Lansing strain of poliomyelitis virus. The titre in the brain decreased over a period of approximately 6 hours, and then rose rapidly during 12 to 18 hours to reach a titre of 10^{-4}. In the spinal cord the same time relations were observed, but the final titre was generally 10 times that in the brain. When a 1% suspension was used for infection the increase in virus titre occurred about 9 hours later, but the rate of increase was the same as with 10% suspension, and the maximum reached was also the same.

In mice showing no signs of paralysis the titre of the central nervous system remained for at least 7 days between $10^{-3·5}$ and $10^{-4·2}$. In mice which became paralysed the titre was consistently higher. *R. Hare*

1207. **The Growth Curve of the Lansing Strain of Poliomyelitis Virus in Mice: the Effect of Sodium Monofluoroacetate and Methionine Sulfoximine on the Early Phase of Growth of the Virus**
J. D. AINSLIE. *Journal of Experimental Medicine* [*J. exp. Med.*] **95**, 9–18, Jan. 1, 1952. 2 figs., 10 refs.

The administration of sodium fluoroacetate probably interrupts the Krebs cycle so that citric acid is not utilized, with a resulting disturbance in cellular function. In this paper from the University of Michigan, Ann Arbor, it is shown that when administered to mice infected with the Lansing strain of poliomyelitis, it has marked effects on the growth of the virus in the brain and cord. After an initial delay of about 6 hours in control animals, the amount of virus recoverable from the brain rises rapidly to a maximum in 24 hours. In mice receiving sodium monofluoroacetate (80 μg. in one experiment and half that dose in the second, injected one hour before virus) the delay period is lengthened to 12 hours, with multiplication beginning at 18 hours; but thereafter the speed of multiplication is the same as in the control animals. *R. Hare*

1208. **Studies on Entry and Egress of Poliomyelitis Infection—IV. Atraumatic Oral Entry: Distribution of Lesions and Virus during the Incubation Period: with Notes on Asymptomatic Poliomyelitis**
H. K. FABER, R. J. SILVERBERG, and L. DONG. *Journal of Experimental Medicine* [*J. exp. Med.*] **94**, 455–470, Dec. 1, 1951. 1 fig., 12 refs.

In this study young monkeys were infected with poliomyelitis by swabbing the mouth and pharynx with a suspension of virus. During the subsequent 2 to 9 days the animals were killed and the distribution of virus observed by histological methods and by attempting to recover the virus from the ganglia supplying the exposed mucous surfaces and from the central nervous system.

Histological signs of infection in all the ganglia examined (Gasserian, petrosal-nodose, superior cervical sympathetic, and coeliac) were present from the 3rd to 7th days, increasing to a maximum on the 5th day and then declining. Sympathetic ganglia showed a secondary increase on the 7th day. Histological reaction was most

severe in the Gasserian ganglion. During the first 7 days no significant signs of infection were noted in the central nervous system. Virus was recovered from the Gasserian ganglia in 3 to 8 days, from the nodosa in 3 to 6 days, but irregularly and infrequently from the sympathetic ganglia. Control animals developed symptoms after an average of 9 days; 2 which remained symptom-free showed histological signs of infection in the Gasserian and other ganglia but none in the central nervous system.

It is concluded that when poliomyelitis virus is placed on the oropharyngeal mucosa it rapidly ascends peripheral nerves and infects their ganglia, where it is localized for several days. Thereafter, virus may invade the central nervous system and produce a paralysis, or it may die out without further spread. In these experiments the Gasserian ganglia appeared to be the most involved and the sympathetic the least in the transmission of virus to the central nervous system. The gustatory nerves evidently played only a minor role. It is suggested that the incubation period may correspond with the time preceding invasion of the central nervous system, when infection is confined to the peripheral ganglia. "Subclinical poliomyelitis" is regarded as a transient infection limited to peripheral ganglia.

[There is a full discussion of the background and interpretation of these experiments which cannot readily be summarized.] *Peter Story*

1209. **The Effects of Cortisone and Adrenocorticotrophic Hormone on Poliomyelitis and on Other Virus Infections**

G. M. FINDLAY and E. M. HOWARD. *Journal of Pharmacy and Pharmacology* [*J. Pharm. Pharmacol.*] **4**, 37–42, Jan., 1952. 1 fig., 3 refs.

Employing the MEF1 strain of poliomyelitis virus, injected intracerebrally into mice in doses of 100 LD50, the authors found that cortisone or ACTH increased the number of deaths and shortened the period of survival very considerably, the effect being most marked with cortisone. Other experiments suggested that the virus in cortisone-treated mice was present in much higher concentrations in the spinal cord 24 and 48 hours after the injection than it was in controls.

The Lansing strain of poliomyelitis virus is generally unable to produce symptoms or kill golden hamsters, but when it was injected into 5 animals receiving cortisone (5 mg. cortisone acetate at the time of injection and another dose 3 hours later) 4 of them became paralysed, on the 3rd, 8th, 11th, and 28th days respectively. In other experiments it was found that cortisone-treated mice died much more rapidly from a viscerotropic strain of Rift Valley fever virus than did controls; and further that the Coxsackie virus multiplies more rapidly, and that the Columbia SK strain of encephalomyocarditis virus produces lesions earlier in cortisone-treated animals.

[These experiments increase the already impressive volume of evidence that cortisone and ACTH have profound effects in increasing the susceptibility of animals to many forms of bacterial and virus infection.] *R. Hare*

1210. **Influenza: a Study of Four Virus Strains Isolated in 1951**

W. SMITH, J. C. N. WESTWOOD, and G. BELYAVIN. *Lancet* [*Lancet*] **2**, 1189–1193, Dec. 29, 1951. 19 refs.

The authors note that antigenic analysis of the two strains of virus A-prime isolated by Andrewes and Isaacs during the 1950–1 influenza epidemic threw no light on the fact that in the Liverpool district the 1950–1 disease was of a severity comparable to that of the 1918–19 pandemic, whereas it was uniformly mild in other parts of the world.

Four new strains were isolated from cases of moderate severity occurring in London in January, 1951, which showed several novel features. Two of them had unusual virulence for the chick embryo, causing a toxaemic type of death within 42 hours after injection into the amnion, and one of these showed a definite neurotropic tendency. The adaptability to mice of these two strains was also exceptional; they produced specific lung lesions from the first intranasal inoculation of allantoic fluid. All four strains differed from previously described strains in their susceptibility to a second haemagglutination-inhibitor in normal rabbit serum, for which the term β-inhibitor is proposed, to distinguish it from the α-inhibitor active against most strains of influenza. The former differs from the latter in being insusceptible to the receptor-destroying enzyme of cholera vibrio toxin, and in being more active against living than against heated virus.

Antigenic analysis by conventional methods showed that, in spite of these unusual characters, the four new strains were all closely related to the standard A-prime virus F.M.1. It is suggested that important variations in biological properties may occur without any detectable antigenic differences, and that to rely exclusively on antigenic analysis in the classification of new strains of influenza virus is a mistake. *M. H. Salaman*

BACTERIA

1211. **The Antistreptococcal Property of Milk—I. Some Characteristics of the Activity of Lactenin *in vitro*. The Effect of Lactenin on Hemolytic Streptococci of the Several Serological Groups. II. The Effects of Anaerobiosis, Reducing Agents, Thiamine, and Other Chemicals on Lactenin Action. III. The Role of Lactenin in Milk-borne Epidemics. The *in vitro* Action of Lactenin**

A. T. WILSON and H. ROSENBLUM. *Journal of Experimental Medicine* [*J. exp. Med.*] **95**, 25–59, Jan. 1, 1952. 37 refs.

Lactenin is a heat-labile antistreptococcal substance present in the milk of cows, goats, and human beings, and was so named by Jones and Simms (*J. exp. Med.*, 1930, **51**, 327). The present authors, working in the Alfred I. du Pont Institute of the Nemours Foundation, Wilmington, Delaware, have re-examined the substance from the point of view of its activity *in vitro* and also of its action on different types of streptococci within the various Lancefield groups. Lactenin is inactivated at a temperature of 80° C., but appears to withstand pasteurization at 61° C. The substance is present in the whey

fraction. It will not pass through a dialysing membrane, and as it is not digested by trypsin, it can be separated from much inert milk-protein if tryptic digestion is followed by dialysis. Lactenin has not been prepared in a pure form and its chemical composition is unknown. In its natural state in raw milk it remains stable for several weeks if stored at 6° C.

Streptococci vary in their sensitivity to this substance. The recordable sensitivity by the tube dilution method takes several hours before it is obvious, but so long as the inoculum is small, fresh raw milk to which the sensitive strains are added is sterilized in 24 hours. All Group-A streptococci are highly sensitive, most strains of Groups B, C, D, and E are resistant, and Groups F, G, H, K, and L are irregular in their reaction to lactenin.

Lactenin is not active under anaerobic conditions, and sulphydryl-reducing substances such as cysteine and glutathione render it inactive. The inactivation of the substance by excess of aneurin, it is suggested, is brought about by the competition for aneurin by the lactenin-sensitive bacterial cell.

Evidence is adduced to explain the rarity of milk-borne epidemics by the ability of lactenin to prevent multiplication of Group-A streptococci when fresh raw milk is contaminated with that organism. Dried milk or condensed milk, the processing of which destroys the lactenin, may, however, be responsible for outbreaks of streptococcal infection in closed communities if contaminated during reconstitution and not used immediately. Although Group-A streptococci are sensitive *in vitro* to the action of lactenin, bovine mastitis can readily be induced experimentally with organisms of this group. The failure of the antistreptococcal substance in such cases appears to be associated with the observation that it was inactive under anaerobic conditions. The authors bring forward supporting evidence with regard to the low oxidation–reduction potential of milk in the cow's udder. There is no evidence that lactenin-containing milk administered orally had any prophylactic or therapeutic effect against Group-A streptococcal infections. *H. J. Bensted*

1212. **Penicillin-resistant Staphylococci. Distribution among Outpatients**
G. A. C. SUMMERS. *Lancet* [*Lancet*] **1**, 135–137, Jan. 19, 1952. 6 refs.

Some authors have already suggested that a hospital is a potential source of penicillin-resistant staphylococci. The present author's findings, based on an investigation of 994 in-patients and out-patients from whom coagulase-positive *Staphylococcus aureus* had been isolated at the Radcliffe Infirmary, Oxford, indicate that the isolation of penicillin-resistant staphylococci is in direct relation to the frequency of attendance at hospital. This was especially obvious among the patients of the ear, nose, and throat, the eye, and the out-patient departments. In patients with open lesions, and to a lesser degree also patients with closed lesions, a 300% increase in incidence of penicillin-resistant staphylococci was found among those who had had frequent contact with the hospital; this applied also to casualty patients.

It is of interest to note that, in the ear, nose, and throat department particularly, there was among patients who frequently attended the hospital a greater increase in the incidence of penicillin-resistant staphylococci in those who had been treated with penicillin (83%) than in those not so treated. *J. W. Czekalowski*

1213. **Effects of Hyperthermia and Antibacterial Agents on Tubercle Bacilli**
J. MARKS. *British Medical Journal* [*Brit. med. J.*] **2**, 1318–1320, Dec. 1, 1951. 3 refs.

About 25% of strains of *Mycobacterium tuberculosis* (human type) grew very poorly in Dubos's medium at 40° C. The growth of the remainder was slightly or moderately impaired. The sensitivity of strains growing sufficiently well for testing at 40° C. was considerably increased to streptomycin, *p*-aminosalicylic acid, and often to thiosemicarbazone, but not to mercuric chloride. Reasons are advanced for trying a combination of hyperthemia with streptomycin and *p*-aminosalicylic acid treatment in tuberculosis of man caused by the human type of bacillus.—[Author's summary.]

SEROLOGY

1214. **Differences in the Behaviour of Sensitized Red Cells to Agglutination by Antiglobulin Sera**
J. V. DACIE. *Lancet* [*Lancet*] **2**, 954–955, Nov. 24, 1951. 5 refs.

In a study of the behaviour of sensitized erythrocytes to agglutination by antiglobulin sera, carried out at the Postgraduate Medical School, London, a preparation of α and β globulin and another of γ globulin were mixed in serial fourfold dilution with equal volumes of a potent antiglobulin serum diluted 1 in 4. After standing for 5 minutes the preparations were tested for their ability to agglutinate a range of sensitized erythrocytes. When erythrocytes sensitized by the cold antibodies present in normal serum were employed, the addition of γ globulin to the agglutinating serum made little difference to its agglutinating effect, but with erythrocytes sensitized by warm antibodies (anti-D and the antibodies from some cases of acquired haemolytic anaemia) the γ globulin was markedly inhibitory. The reactions of preparations with α and β globulin were less clear-cut, and variation may have been due to the presence of traces of γ globulin. *John F. Loutit*

1215. **Demonstration of Multiple Antibodies in Antiglobulin Sera**
H. CRAWFORD and P. L. MOLLISON. *Lancet* [*Lancet*] **2**, 955–957, Nov. 24, 1951. 3 refs.

In experiments by the Medical Research Council's Blood Transfusion Research Unit at the Postgraduate Medical School of London samples of antiglobulin serum were prepared from rabbits immunized with human serum, heated to destroy complement, and absorbed with normal human erythrocytes of Groups A, B, and O. The serum was again absorbed with different sensitized human erythrocytes. After absorption with

Rh-sensitized erythrocytes a sample of serum still agglutinated Group-A-sensitized erythrocytes, normal cold-sensitized erythrocytes, and the erythrocytes from 2 cases of acquired haemolytic anaemia. Conversely, when a serum was absorbed with normal cold-sensitized erythrocytes, it still agglutinated Rh-sensitized and A-sensitized erythrocytes and erythrocytes from cases of acquired haemolytic anaemia. After absorption with the erythrocytes from one case of acquired haemolytic anaemia the serum still agglutinated erythrocytes from another case and the artificially sensitized erythrocytes.

John F. Loutit

1216. **Clinical Evaluation of the Middlebrook–Dubos Hemagglutination Test**

R. M. YOUNG and W. A. LEONARD. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **21**, 1045–1050, Nov., 1951. 4 refs.

A haemagglutination test for the detection of antibodies in the serum of patients infected with tubercle bacilli has been described by Middlebrook and Dubos, and modified by Smith and Scott. A clinical evaluation of this test was made by examining the serum of 547 persons at the Rhode Island Hospital to determine whether a given titre is significant, and to correlate the serum titre of haemagglutinins with the activity of tuberculosis.

Sheep's blood was diluted with equal quantities of modified Alsever's solution. The blood was washed and centrifuged with 5 volumes of phosphate-buffered saline. The serum for testing was diluted with phosphate-buffered saline and inactivated by heating. To remove heterophile antibodies from the serum, 0·4 ml. of normal unsensitized erythrocytes were added to each tube and, after standing, removed by centrifugation. The sheep erythrocytes were sensitized by adding the cells in amounts of 0·1 ml. to 6 ml. of a 1 in 12 dilution of tuberculin. After being incubated and centrifuged the supernatant fluid was removed and the cells resuspended in buffered saline; this was repeated three times and the suspension was then stored at 4° C. and used within 3 days.

To carry out this test, two-fold serial dilutions (ranging from 1 in 2 to 1 in 128) of the serum were made in phosphate-buffered saline. To each dilution 0·4 ml. of a 0·2% suspension of sensitized erythrocytes was added. A control to detect incomplete absorption of heterophile antibodies was used for each serum, and one to detect spontaneous clumping of sheep's cells for each group of tests. The tubes were agitated, incubated at 37° C. for 2 or 3 hours, and then allowed to stand overnight at room temperature. A positive result was indicated by clumping of cells or by a granular appearance.

Of 83 patients with active pulmonary tuberculosis 66 showed a titre of haemagglutinins at 1 in 8 or higher, and a positive test at 1 in 2 or greater was obtained in 74 of these. Of 19 patients with extrapulmonary tuberculosis, only 1 gave a negative result. Serum from 34 cases of arrested tuberculosis were tested and 28 were positive at titres of 1 in 2 or higher; 411 non-tuberculous patients were tested; 30% had no haemagglutinins, but the remainder gave a positive reaction.

The test may thus on occasions be of use in excluding tuberculosis, although occasionally a patient with active disease may not possess haemagglutinins if he is extremely ill. A positive reaction with a serum dilution of less than 1 in 8, or a negative reaction, tends to rule out active tuberculous infection.

T. M. Pollock

1217. **The Differential Test for Infectious Mononucleosis**

I. DAVIDSOHN, K. STERN, and C. KASHIWAGI. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **21**, 1101–1113, Dec., 1951. 1 fig., 29 refs.

The authors discuss the difficulty of the diagnosis of infectious mononucleosis with particular reference to a series of 106 patients, in 63 of whom 26 other diseases had been diagnosed before serological tests had been carried out. The standard Paul–Bunnell test is regarded as non-specific, and is referred to by the authors as the " presumptive test "; specificity is obtained by absorbing the serum with guinea-pig kidney and bovine erythrocytes—a method which is referred to as the " differential test ". The value of the latter test is illustrated by the results obtained in 283 cases of infectious mononucleosis, in which complete absorption with bovine erythrocytes and incomplete absorption with guinea-pig kidney were obtained in all cases. In 4 tests antibody was completely removed by both procedures from patients with serum disease, and similar results were obtained in 304 control tests in healthy subjects or in patients with other diseases.

The distribution of titres obtained in 403 presumptive tests on the 283 patients with infectious mononucleosis is shown diagrammatically; the reaction was negative, with titres of 1 in 28 to 1 in 112, in 91 instances (22·6%), but the diagnosis was confirmed by a positive result in the differential test. The results with 7 patients showed that a negative reaction obtained in the first week of illness might become positive a few days later. In 19 patients examination was carried out at intervals until the differential test became negative; negative results were obtained in 11 patients by the 12th week after the onset of illness and in one patient after 4½ weeks, whereas one patient still gave a positive result after 18 weeks.

The authors strongly defend the merits of the differential test, and regard the unsatisfactory results with the heterophile antibody tests obtained by other workers as due to their use of the presumptive test alone. They point out that the differential test can be simplified by reading the tubes after 15 minutes, when positive results may already be obtained, and also by reducing the guinea-pig kidney absorption period to 3 minutes. The presumptive test should be used in cases in which infectious mononucleosis is suspected on clinical or haematological grounds, and a titre greater than 1 in 224 is accepted as positive. The differential test may be used when the titre is less than 1 in 112, when it is higher than 1 in 56 in the presence of typical signs, or when the patient has recently had an injection of horse serum.

D. J. Bauer

Hygiene and Public Health

1218. **The Spread of Infantile Gastro-enteritis in a Cubicled Ward**

K. B. ROGERS. *Journal o Hygiene* [*J. Hyg., Camb.*] **49**, 140–151, June–Sept., 1951. 9 figs., 19 refs.

The α and β types of *Bacterium còli* were used as "indicator organisms" in an attempt to observe the mode of transmission of infantile gastro-enteritis in cubicled wards at the Children's Hospital, Birmingham. Experience in a three-floor hospital block showed that cross-infection between different floors did not occur unless patients were transferred from one to another. This fact suggested that articles in communal use within a ward unit were responsible for the transmission of infection. It was shown that during ordinary nursing routine, such as bed-making, napkin-changing, weighing, and feeding, the indicator organisms were thrown up into the air. Floor dust, the bath and its plug, cot sides, thermometers, hand towels, and other articles were found to be heavily contaminated; contamination of a cubicle was shown to occur within a few hours of the admission of a child harbouring a type strain; and the organisms could survive in infected dust for many days. Ward articles remained infected even after washing with 5% lysol and subsequent drying. *W. G. Harding*

1219. **Inter-hospital Cross-infection of Epidemic Infantile Gastro-enteritis associated with Type Strains of *Bacterium coli***

K. B. ROGERS and S. J. KOEGLER. *Journal of Hygiene* [*J. Hyg., Camb.*] **49**, 152–161, June–Sept., 1951. 3 figs. 2 refs.

The spread of infection between three Birmingham hospitals was studied, the α and β types of *Bacterium coli* being used as "indicator organisms". In 3 cases epidemics were found to have been spread between hospitals by the transfer of patients, and the danger of the spread of gastro-intestinal infection through hospital out-patient departments as well as wards is stressed. In view of the close association of outbreaks of infantile gastro-enteritis with the α and β types of *Bact. coli* it is suggested that the faeces of all infants should be examined bacteriologically as a routine on admission to a hospital, and that institutional outbreaks should be notified to a central bureau for the information of other hospitals and paediatric centres. *W. G. Harding*

1220. **Endemic Infectious Hepatitis in an Infants' Orphanage—I. Epidemiologic Studies in Student Nurses**

R. B. CAPPS, A. M. BENNETT, and J. STOKES. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 6–23, Jan., 1952. 8 figs., 16 refs.

Between 1942 and 1949, 75 cases of acute infective hepatitis occurred among adults in an orphanage for infants and small children, and in July, 1949, an investigation was started with the aim of finding out how this infection was kept alive and its means of spread. The 5-storey orphanage housed an average population of 180 children under 3, 15 unmarried expectant mothers (admitted for the last 2 to 4 months of pregnancy), 25 to 30 maternity cases (admitted for delivery only), 50 student nurses, 20 graduate nurses, and 10 domestic servants. The orphans remained sometimes for 1 to 2 years, but usually for about 4 months, while the student nurses trained for one year.

Of the 75 cases of hepatitis, 72 were in student nurses. There were no cases among the expectant mothers or maternity cases, so that spread by water or food from the central kitchen was eliminated. The possibility of parenteral transmission was also eliminated, so that spread by person-to-person contact was established. From September, 1949, serial clinical and laboratory investigations were made on as many children as possible, and subclinical infectious hepatitis was found to be prevalent on all floors. Only in one of the 25 cases thus diagnosed did the patient show any jaundice. Conclusive proof that the children were infected was provided when adult volunteers contracted hepatitis after swallowing filtered faecal material from 2 of these cases. It was observed that student nurses who worked in wards on the fourth floor subsequently developed hepatitis, and it was found that on this floor attention to details of hygiene by the student nurses was particularly bad. Special attention was therefore paid to asepsis on this floor, and after the expected lag period for incubation of one month, no further new cases appeared.

Only one of 35 nurses given gamma globulin on entry contracted hepatitis; 21 of these nurses were assigned to the fourth floor 6 months after receiving the injection, and there was evidence that some developed subclinical hepatitis and subsequent active immunity.

Jessie Freeman

1221. **Observations on the Incidence and Distribution of the Common Cold in a Rural Community during 1948 and 1949**

O. M. LIDWELL and T. SOMMERVILLE. *Journal of Hygiene* [*J. Hyg., Camb.*] **49**, 365–381, Dec., 1951. 1 fig., 5 refs.

A study of the occurrence of the common cold in a Wiltshire village during the years 1948 and 1949 showed that, in this community, school children experienced about three times as many colds as adults living in households without school children, and that the presence of school children in the household approximately doubled the numbers of colds experienced by both adults and infants under 5 years of age.

More detailed analysis suggests that the school children acquired infections outside the household three times as frequently as did the adults and nearly twice as frequently as the infants, but that the infants were more than twice as susceptible as school children or adults to

cross-infection within the household. The distribution of multiple infections in households conforms to that which would be expected if subsequent infections were as likely to infect the remaining uninfected members of the household as the first infected individual introduced into the household. The risk of such cross-infection by exposure to infections within the same household appears to be about 1/5.—[Authors' summary.]

1222. **An Outbreak of Q Fever in East Kent**
M. S. HARVEY, G. B. FORBES, and B. P. MARMION. *Lancet* [*Lancet*] **2**, 1152–1157, Dec. 22, 1951. 3 figs., 18 refs.

This is the first account of an explosive outbreak of Q fever in Britain. During June, 1950, 27 full-time students and a caretaker at an art college in Canterbury fell ill over a period of 10 days. The symptoms included rapidly developing fever (in 23), severe headache (in 21), retro-orbital pain with photophobia and, sometimes, injection of the conjunctivae (in 12), neck stiffness (in 11), and respiratory symptoms (in 5). Serological examination was carried out early in the disease in 6 of the cases, and complement-fixation tests showed rising titres for *Rickettsia burnettii*. The results of serological investigation in the remainder of the cases, which was largely retrospective, were also positive. In 9 out of 20 volunteer day students who had had no symptoms the results of a similar investigation were positive, with lower titres for *R. burnettii* than those obtained in the patients. Inquiry among the college staff and the evening students revealed no other cases, but one man from the town, whose place of work adjoined the college and who regularly parked his car at the rear of the main college building, became ill at the same time as the students.

Epidemiological investigations excluded case-to-case spread, contact with cows, sheep, and goats, visits to potentially infected environments, consumption of raw milk, and bites of insects. Other investigations suggested that a packing case, which was broken up in the college buildings some 19 days before the outbreak occurred, may have contained infective material.

W. G. Harding

1223. **A Comparison of the Trends of Male and Female Mortality**
W. J. MARTIN. *Journal of the Royal Statistical Society* [*J.R. statist. Soc.*] **114**, 287–306, 1951. 5 refs.

1224. **Fatality and Survivorship in Pulmonary Tuberculosis. A Study of Notified Cases in Edinburgh: 1936–44**
M. S. ACKERS. *Edinburgh Medical Journal* [*Edinb. med. J.*] **58**, 489–502, Oct., 1951. 1 fig., 6 refs.

"Nominal fatality" from pulmonary tuberculosis in Edinburgh for the periods 1936–9, 1942–4, and 1946–9 was 61·2%, 53·8%, and 47·8% respectively. (Nominal fatality is defined as the ratio of deaths from pulmonary tuberculosis in a given year to the mean of the notifications in that year and the preceding one, expressed as a percentage.) During the periods investigated the number of deaths remained the same, but the number of notifications increased. In all three periods and for both sexes the nominal fatality increased with increasing age of notification. The fall in nominal fatality from 1936 to 1949 was most marked in both sexes in the age group 15 to 34 and also in males of age group 35 to 64.

Because of the long and variable duration of the illness, nominal fatality gives only a rough measure of the true fatality from pulmonary tuberculosis. A better measure is given by the number of survivors in successive years after the notification of the disease. Of 3,969 notification in 1936–44, in 76% the patient was alive after the first year and in 67% after the second, the figure then falling regularly to 50% alive after the 7th year. In males the younger age groups showed a significantly better survival rate than the older ones, but there was little difference for females. Under the age of 34 the male survival rate was better than the female, but over this age the position was reversed. For both sexes the survival rate was better for cases notified in 1942–4 than for those notified in 1936–9.

Year-to-year survivorship—that is, the ratio of the number alive at the end of a year to the number alive at the beginning of that year—showed that the greatest mortality occurred during the first year after notification and increased markedly with age, particularly in males. For males the mortality in the second year was still appreciable, whereas for females the period was 3 to 4 years. After this time the effect of age in increasing the death rate became less marked. The year-to-year survivorship ratios show how deaths during the first year after notification dominate the figures for later years, thereby making nominal fatality figures unreliable.

The improvement in fatality rates during the latter part of the period does not necessarily mean a decline in severity of the disease. Because of improvements in diagnosis and therapy, and the introduction of mass radiography in 1945, the periods are not comparable. However, the age and sex difference in survival rate, which are independent of these changes, seem to be real.

M. Lubran

1225. **Sterilization of Woollen Fabrics**
H. F. BARNARD. *British Medical Journal* [*Brit. med. J.*] **2**, 21–24, Jan. 5, 1952. 3 figs., 31 refs.

The majority of freshly laundered hospital blankets were found to harbour *Staphylococcus aureus*, the organism readily surviving the laundering process. It was also found that during laundering the bacteria passed from contaminated to uncontaminated blankets. As this might be a possible route of spread of penicillin-resistant staphylococci in hospitals it appeared desirable to sterilize blankets.

Cetyl pyridinium bromide was used to treat contaminated blankets which were not oiled, and its activity was judged from the number of colonies of staphylococci that appeared on blood agar over which the blanket was shaken. When the blanket was shaken over plates sown with a culture of *Staph. aureus* areas of inhibition of growth appeared round the fibres which alighted on the plate.

The treatment is considered to be effective and cheap.

Scott Thomson

Industrial Medicine

1226. **Rheumatism in Miners—I. Rheumatic Complaints**
J. S. LAWRENCE and J. AITKEN-SWAN. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **9**, 1–18, Jan., 1952. 3 figs., 8 refs.

An investigation has been made into the incidence of rheumatic complaints in miners by means of a field survey arranged to include control groups of non-mining males and of females from mining and non-mining families. The gross incidence of rheumatic complaints was not found to be appreciably different in miners and non-miners, but there was evidence of an earlier onset in miners, as shown by a higher incidence in the fourth decade. The miners' statements indicated that they lost more working time from rheumatic complaints than non-miners. Rheumatic pain in miners was chiefly in the lumbar and sciatic distribution, and pain in these sites was largely accounted for by the increased incidence of rheumatic complaints in the fourth decade and for the increased loss of working time in miners. Miners also showed an increased incidence of knee pain. Tentative diagnoses made in the field indicated that the lumbar sciatic pain may frequently result from disorders of the intervertebral discs. There was also evidence of an increased incidence of osteo-arthritis in the miners. A study of invaliding records made under the Essential Works Order showed that invaliding from the mines was due most commonly to chest conditions, rheumatism coming second in importance. Those invalided for rheumatism complained chiefly of low-back sciatic pain. The incidence of rheumatic complaints in members of the miners' families was lower than in the general populations and considerably lower than in miners.—[Authors' summary.]

1227. **Silicosis in the Ball-clay and China-clay Industries**
R. W. THOMAS. *Lancet* [*Lancet*] **1**, 133–135, Jan. 19, 1952. 2 figs., 8 refs.

The production of ball clay and china clay in mines and quarries is not a dusty occupation, and there is no evidence that workers engaged in these mines and quarries have ever suffered from pneumoconiosis. On the other hand, the preparation of these materials for use in industry by grinding and bagging for transport may expose workers to high concentrations of dust; but hitherto no reports of pneumoconiosis from these causes have been reported. Two such cases are now presented.

The first man died at the age of 64. He had spent nearly all his working life in the ball-clay industry, much of it in drying-kilns and grinding-mills. He developed shortness of breath, and on radiological examination a picture suggesting nodular silicosis was seen. Necropsy revealed classical silicotic nodulation, mostly in the upper parts of the lungs, without tuberculosis. The second case was in a china-clay worker. His industrial history was not known precisely, but for 5 years before death he had been employed in trucking dry china clay from the drying-kilns to the mill-house. He had also been concerned with the grinding of china stone and felspar many years previously. He died suddenly. At necropsy tuberculo-silicotic masses with moderate numbers of small classical silicotic nodules were found.

It is clear that the silicosis in the first case was attributable to ball clay, which may contain up to 29% free silica. The silico-tuberculosis of the second case cannot be definitely attributed to china-clay dust, for the man had had a mixed industrial history.

The author suggests that further investigation is required of men exposed to china-clay and ball-clay dusts. *C. M. Fletcher*

1228. **Current Concepts of Beryllium Poisoning**
H. S. VAN ORDSTRAND. *Annals of Internal Medicine* [*Ann. intern. Med.*] **35**, 1203–1217, Dec., 1951. 15 figs., 21 refs.

In this review of the subject the clinical aspects of beryllium poisoning are discussed and are illustrated by reference to the author's series of 450 cases. A brief description of the properties and uses of beryllium and its compounds is given.

Beryllium causes two types of skin lesion. The commonest manifestation is a contact dermatitis, which is eczematous in type and has been shown to be due to hypersensitivity. The skin of affected individuals gives a positive reaction to patch tests with high dilutions of beryllium compounds. The second type of skin lesion is a chronic granuloma, which appears to be a local reaction following accidental implantation of beryllium compounds at the site of an abrasion. The granuloma is cured by excision.

The respiratory tract may exhibit an acute reaction to beryllium and its compounds, which may consist in minor upper respiratory symptoms or in a pneumonitis which has been called "acute berylliosis". The latter condition begins with cough and dyspnoea, and after 2 or 3 weeks radiological examination shows symmetrical infiltration of both lung fields. The author had 98 cases of this type, 12 of which ended fatally. Death occurs about 30 days after the onset of the illness, and is due to asphyxia with or without acute cor pulmonale. In the non-fatal cases complete recovery occurs within 4 months, and over a 10-year period there has been no evidence that the chronic type of pulmonary disease supervenes in the recovered cases. Hyperglobulinaemia and diminished liver function have been demonstrated during the acute illness, and pathological studies show an intra-alveolar odematous exudate in the lungs, with centrilobular necrosis in the liver.

The chronic form of respiratory involvement appears some time after exposure, even up to 10 years later. Radiological changes, consisting of disseminated fine

nodular infiltration, precede the development of symptoms. The latter are similar to those of acute berylliosis with the addition of anorexia and weight loss, and intermittent fever occurs in a few cases. Though the chronic disease does not progress so rapidly as the acute form, the outlook is sombre. One-third of the author's patients died and another third showed steady deterioration. The pathological changes affect the interstitial tissues of the lungs, and consist of a chronic, sarcoid-like granulomatous infiltration. Beryllium has been found in renal calculi, lymph nodes, and the liver. Death is due to chronic cor pulmonale.

The conclusion reached by both Machle and Hardy that beryllium poisoning is a systemic disease is accepted, and some discussion follows on the possible physiopathological mechanisms involved. Although toxic effects in the lung, liver, and kidneys of animals have been produced, nothing resembling chronic berylliosis in man has been seen. Gardner *et al.* have produced osteogenic sarcomata in rabbits by injecting beryllium compounds, but such lesions have not been found in man. The radioactive isotope ^{7}Be has been shown to enter the bones of small animals, and this fact has suggested the hypothesis that chronic berylliosis may occur as a result of the release of beryllium from the bones following various stresses occurring at a later date. The observation by Curtis that the acute eczematous contact dermatitis is due to hypersensitivity has led to the suggestion that acute berylliosis may have a similar aetiology. Other experimental observations have shown that beryllium replaces magnesium in various enzyme systems which subsequently become inhibited, and this has been adduced as evidence that the manifestations of chronic berylliosis may be due to widespread cellular changes.

Although ACTH and cortisone have been shown to be of great benefit in treatment of chronic berylliosis, emphasis is laid on the importance of engineering methods of control of beryllium exposure in industry.

W. K. S. Moore

1229. **Vanadium Poisoning from Cleaning Oil-fired Boilers**
N. WILLIAMS. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **9**, 50–55, Jan., 1952. 2 figs., 5 refs.

Crude-oil ash, according to its source, may contain as much as 45% vanadium compounds. Fuel oils are produced after distillation of the more volatile hydrocarbons, and their content of vanadium is, therefore, even higher than that found in the corresponding crude oil. A significant amount of vanadium pentoxide accumulates in soot in the gas passages of boilers, and these have to be cleaned once a year, thus exposing boiler-cleaners, bricklayers, and scaffolders to the dust hazard. Before London Transport Executive's boilers were converted to oil-firing no complaints were received from boiler-cleaners, but since that time symptoms, undoubtedly due to the work, occurred regularly.

In this paper 8 cases are reported, and the author describes his own experience following exposure during boiler-cleaning. Rhinorrhoea, sneezing, and watering of the eyes occurred within an hour or two. This was followed in a few hours by a dry cough, wheezing, dyspnoea, and retrosternal soreness. Dyspnoea and depression continued and the cough rapidly became productive. Clinically, rhonchi were audible over both lung fields, blood pressure appeared to be lowered, and there was a characteristic greenish-yellow coating on the tongue. In 2 cases vanadium was excreted in the urine, and in 2 others a fine tremor of the hands was noted. Thermal precipitation samples of atmospheric dust in the boilers were examined, particle size varying from below 1μ up to 11μ in diameter, 93·6% being below 1μ. Analysis of the dust in the combustion chamber showed a vanadium content of 58·6 mg. per c. metre of air.

Among preventive measures instituted were the use of compressed-air jets from outside the chamber, the wearing of dust respirators by men who had to enter the boiler, and water-spraying before removal of bricks. These methods were successful in overcoming the incidence of vanadium poisoning, and no complaints were received during the cleaning of two boilers under these conditions.

A. Lloyd Potter

1230. **Polymer-fume Fever**
D. K. HARRIS. *Lancet* [*Lancet*] **2**, 1008–1011, Dec. 1, 1951. 12 refs.

Polymerization of tetrafluorethylene produces an inert plastic which is unusually thermostable. This polytetrafluorethylene (" teflon " or " fluon ") gives off an invisible toxic fume when heated above 300° C., when extruded hot, or when heated by friction with cutting tools. After a few hours' latent period, exposed workers may experience an influenza-like illness, with retrosternal oppression, dry cough, and malaise, followed by fever up to 104° F. (40° C.), rigors, and sweating. There are sometimes transient signs in the chest. Spontaneous recovery takes place in about 2 days.

Experiments on rats showed that exposure to fluon heated to between 140° and 325° C. produced respiratory irritation and death from pulmonary oedema and haemorrhage, especially in experiments at over 300° C. An unidentified mineral acid was evolved, and also, at the latter temperature, a sublimate. Decomposition at 600° to 700° C. produces C_2F_4, C_3F_6, and C_4F_8, but these are not toxic.

The exact nature of the toxic substance in this case is not yet known; a parallel is drawn with metal-fume fever, but only very small quantities of metals were found in the polymer ash. Prevention is by local exhaust ventilation. Treatment is symptomatic, and oxygen is recommended. Some doubt exists whether symptoms can arise from inhaling cold polymer dust.

Full details are given of 2 cases in men exposed to the fume, both of whom had had several attacks.

J. N. Agate

1231. **Tetryl Toxicity: a Summary of Ten Years' Experience**
B. B. BERGMAN. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **5**, 10–20, Jan., 1952. 17 refs.

Forensic Medicine and Toxicology

1232. **The Differential Diagnosis between Suicide, Homicide, and Accident in Lesions due to Explosives.** (Criteri diagnostici differenziali fra suicidio, omicidio ed accidente nelle lesioni da ordigni esplosivi)
G. GUARESCHI. *Minerva Medicolegale* [*Minerva medico-leg., Torino*] **71**, 89–96, July–Aug., 1951. 4 figs., 16 refs.

The differential diagnosis between suicide, homicide, and accident in lesions due to explosives is discussed by reference to cases described in the literature and from the records of the Medicolegal Institute of Parma. The information thus collected with regard to the site and distribution of the lesions is summarized in diagrammatic form.

In suicide the important lesions are almost exclusively in the head (15 out of 22 cases) or parts of the body containing vital organs. In accidents the lesions are common in the hand which manipulates the explosive or scattered irregularly in various parts of the body. In criminological practice homicidal lesions by explosives are very uncommon, and can usually be clearly distinguished from those of suicide by their site and distribution, but rarely from those of an accident.

F. A. Langley

1233. **The Surgery of the Hymen: Medico-legal Aspects.** (Chirurgia dell'imene: aspetti medico-legali)
R. POZZATO. *Minerva Medicolegale* [*Minerva medico-leg., Torino*] **71**, 100–104, July–Aug., 1951. 7 refs.

The commonest cause of non-sexual defloration is hymenotomy preliminary to a diagnostic or therapeutic intervention. The legal importance of obtaining consent for this operation is stressed, and also of acquainting the patient of its consequences if an action for nullity of marriage is brought on the grounds of non-consummation. This is especially important in view of the similarity in appearance between a hymen deflowered sexually and one deflowered surgically.

It is suggested that after surgical intervention the hymen should be partially repaired. *F. A. Langley*

1234. **The Identification of Metaldehyde by Koflers' Micro Method.** [In English]
K. TEUCHNER. *Acta Pharmacologica et Toxicologica* [*Acta pharmacol., Kbh.*] **8**, 79–81, 1952. 1 fig., 4 refs.

A method is described for the qualitative identification of metaldehyde occurring in small quantities in gastro-intestinal contents in cases of poisoning. The suspected material is heated to 130° to 140° C. in a subliming glass covered with a coverslip, when metaldehyde, if present, sublimes on to the coverslip at 112° C.

Closer identification is achieved by the method of eutectic temperature. The eutectic temperature is the temperature at which any mixture of two substances begins to melt, and it is constant and characteristic for any given pair of substances. Metaldehyde mixed with β-naphthol or pyrogallol gives mixtures with eutectic temperatures of 115° and 128° C. respectively. In order to observe the melting-point, the coverslip, with sublimate upon it, is inverted on to a slide bearing a few crystals of β-naphthol or pyrogallol, and the preparation is placed on the heating stage of a microscope. At the melting-point of the mixture, drops appear at points of contact between particles of the two substances.

This method gives a clear distinction between metaldehyde and benzoic and salicylic acids, which also sublime from stomach contents. *W. K. S. Moore*

1235. **Sulfhemoglobinemia: a Study of 62 Clinical Cases**
R. O. BRANDENBURG and H. L. SMITH. *American Heart Journal* [*Amer. Heart J.*] **42**, 582–588, Oct., 1951. 14 refs.

The clinical findings in 62 patients admitted to the Mayo Clinic with sulphaemoglobinaemia are discussed with particular reference to the ingestion of drugs acting as causative agents. In all cases the diagnosis was confirmed spectroscopically, and the concentration of sulphaemoglobin varied from 0·25 to 10 g. per 100 ml. of blood. The majority of patients appeared to be neurotic individuals, and the drugs taken included: compounds containing aspirin, phenacetin, and caffeine; acetanilide; "bromo-seltzer"; and sulphonamides in a small percentage. Bromo-seltzer was taken habitually by 60% of the patients, and a high blood bromine level with signs of intoxication was common. Cyanosis was detected in all 14 patients who had 2 g. or more sulphaemoglobin per 100 ml. of blood, and in 33 out of 48 patients who had less than 2 g. per 100 ml.

No significant anaemia was found and no cases of agranulocytosis or neutropenia occurred. Constipation was present in 11 of the 14 patients with 2 g. sulphaemoglobin per 100 ml. of blood, but in only 15 out of the 48 who had lower values. Little or no respiratory distress was noted in 2 patients who had a very high blood level of sulphaemoglobin and severe cyanosis. Comparison of spectrometric readings with functional studies of the oxygen-carrying power of haemoglobin on the one hand, and with clinical evidence of respiratory embarrassment on the other, suggests that the quantitative spectroscopic determinations of sulphaemoglobin may have been somewhat inaccurate.

The authors conclude that sulphaemoglobinaemia is commoner than methaemoglobinaemia, and that continual ingestion of bromides is a potent cause in neurotic individuals, who tend to suffer more from the effects of chronic bromism than from those of the attendant sulphaemoglobinaemia. *J. F. Goodwin*

1236. **Agranulocytosis during Treatment with Diethazine Hydrochloride**
G. C. HELLER and D. A. SIME. *Lancet* [*Lancet*] **1**, 192–193, Jan. 26, 1952. 7 refs.

Radiology

1237. **Protection against *X*-ray and Beta Radiation. Lead Glass Fabric**
V. W. ARCHER, G. COOPER, J. G. KROLL, and D. A. CUNNINGHAM. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 106–108, Jan. 12, 1952. 6 figs., 5 refs.

The authors consider that the proved increase in the incidence of leukaemia among radiologists warrants the search for a more efficient form of protection from stray radiation. This paper reports an investigation into the value of a fabric woven from spun glass containing lead. Tests were made using dental film partly uncovered and partly covered by 1-, 2-, and 3-ply glass fabric. These were placed on various sites over the body surface of a radiologist while he carried out 43 fluoroscopic examinations. The tube was energized at 72 kV (peak) and 5 mA for a total period of 2 hours.

Results showed that unprotected parts of the body received a dose of up to 350 milliroentgens (mr). Where the film was protected by the lead-glass fibre it received 35 mr when protected by one layer, and as little as 9 mr when 3-ply material was used. The authors recommend a gown made up with various thicknesses of material, being of maximum thickness over the abdomen. This garment weighs 10½ lb. (4·76 kg.), is completely flexible, and allows the weight to be partly taken by the shoulders and partly by drawing in and belting at the waist. The gown is washable and is very durable to flexion stresses. The material would also be of value for protective curtaining, both against *x*-radiation and against the beta-radiation from fission products.

A. M. Rackow

EXPERIMENTAL RADIOLOGY

1238. **The Uses of Nuclear Disintegration in the Diagnosis and Treatment of Brain Tumor**
W. H. SWEET. *New England Journal of Medicine* [*New Engl. J. Med.*] **245**, 875–878, Dec. 6, 1951. 5 figs., 7 refs.

In this paper is summarized the work done by the author in collaboration with Selverstone in the use of a very fine probe counter for the location of brain tumours at operation following the injection of radioactive phosphorus. The author goes on to discuss the use of radioactive potassium—a gamma-ray emitter—for detecting the position of brain tumours through the intact skull.

Finally, an account is given of the attempt to locate brain tumours by means of boron, which disintegrates after capturing slow neutrons, giving rise to positrons, and by the use of annihilation radiation in the form of a pair of gamma rays which proceed in opposite directions and can be picked up in a coincidence-counting circuit. (This technique is similar to one developed at Duke University, Durham, N.C.) So far experiments have been carried out with borax, with which the author finds that the necessary levels are obtainable in tumour tissue without giving rise to toxic effects. *D. Waldron Smithers*

1239. **Induction of Thyroid Cancer in the Rat by Radioactive Iodine**
R. C. GOLDBERG and I. L. CHAIKOFF. *Archives of Pathology* [*Arch. Path., Chicago*] **53**, 22–28, Jan., 1952. 3 figs., 9 refs.

An investigation was carried out into the induction of thyroid tumours in rats by injections of single doses of radioactive iodine. Thyroid tumours were found in 9 of 25 rats killed from 1½ to 2 years after a single intraperitoneal injection of 400 microcuries of ^{131}I. Thyroid adenomata were found in 5 rats, 3 of which also had malignant tumours. Malignant thyroid neoplasms—alveolar adenocarcinoma, papillary adenocarcinoma, small-cell carcinoma, and spindle-cell carcinoma—were found in 7 rats; metastases occurred in 5 of these.

Since the incidence of carcinoma of the thyroid gland, even in old rats, is extremely low, this experiment is taken as indicating the production of thyroid carcinoma by radioactive iodine. Evidence is further produced that thyrotrophic hormone is not the causative agent, which, it is suggested, is the ionizing radiation trapped in the gland by the localization of the iodine.

D. Waldron Smithers

1240. **Preparation of Clean Chemical Solutions. With Special Reference to Radioactive Phosphorus Solutions for Clinical Use**
G. E. HARRISON and W. H. A. RAYMOND. *British Medical Journal* [*Brit. med. J.*] **2**, 930–932, Oct. 20, 1951.

In this paper from the Medical Research Council Radiobiological Research Unit at Harwell is discussed the importance of clean radioactive solutions in biological and medical investigations. The achievement of standard dosage is difficult if part of the radioactivity is in a particulate form, as unsuspected localization of the particulate material may occur after injection [see Abstract 1241], resulting in uncertainty regarding the dosage delivered to a particular organ. Experiments with radioactive phosphate solutions are described. Up to the end of 1950 the solutions dispensed were faintly hazy, and on centrifugation at 2,500 revolutions per minute (r.p.m.) for 15 minutes, up to 50% of the radioactivity could be removed in the centrifugate. The methods of dispensing the solutions and cleaning the glassware were changed to minimize bacterial contamination and to reduce particulate inorganic matter and organic substances, and with the new technique (details of which are given), it was found that centrifugation at 2,500 r.p.m. for 20 minutes resulted in a loss of less than 2% of the radioactivity in the centrifugate. *Edward M. McGirr*

1241. **Some Autoradiographic Studies of Non-uniform Distribution of Radioactive Phosphorus in Tissues**
L. F. LAMERTON and E. B. HARRISS. *British Medical Journal* [*Brit. med. J.*] **2**, 932–936, Oct. 20, 1951. 8 figs., 4 refs.

In this paper from the Royal Cancer Hospital, London, are recorded the results of autoradiographic studies on rat and human tissue after injection of radioactive phosphorus (^{32}P) intravenously. Autoradiographs of liver, spleen, bone marrow, and lung showed an irregular spotty appearance due to local high concentrations of the isotope. When the injection was given intraperitoneally no such spotty distribution was evident. The radioactivity of the injected solutions was to some extent concentrated on particulate matter, as contact autoradiographs of dried smears of the solutions gave clear evidence of the presence of concentrations of activity. It was found that appreciable amounts (up to 30%) of the radioactivity could be removed from the solutions by centrifuging at 2,000 revolutions per minute for 30 minutes, and that after injection of the supernatant fluid very few concentrations were seen in liver or spleen. When solutions were prepared by the method of Harrison and Raymond [Abstract 1240] there was usually little or no "spottiness" after intravenous injection, and where "spottiness" did occur it was probably the result of a concentration of radioactivity on particulate material which contaminated the syringe. Rinsing the syringe with 10% phosphate carrier to saturate any such particles with inactive phosphate before filling with the radioactive solution reduced the "spottiness" to very small proportions.

The presence of particulate matter in radioactive solutions obviously influences the distribution and concentration of the isotope in the tissues, depending on the method of administration. This non-uniformity of the radioactivity may affect considerably the dosage distribution in a tissue. An illustrative calculation is presented to give some indication of how the dose will vary throughout a tissue if a beta-ray emitter is distributed in localized sources of high concentration.

Edward M. McGirr

1242. **Radioisotope Hazards and Protection in a Hospital**
M. BRUCER. *Journal of the American Medical Association* [*J. Amer. med Ass.*] **147**, 1745–1751, Dec. 29, 1951. 6 figs., 3 refs.

A report on possible hazards from radioactive isotopes and some methods of protection in hospitals is given by the author from Oak Ridge Institute of Nuclear Studies. The problems arose owing to the increasing use of radioactive substances simultaneously for treatment and for investigation of patients. The method of dealing with these substances is constantly changing, but the techniques found useful by the author are described. The vulnerable period is after the radioactive material has been injected into the patient. As data for permissible doses is still scanty, the levels of safe exposure agreed at the Chalk River Conference (1949), namely, 0·3 r.e.p. per week, equivalent to 6·25 milliroentgens per hour, were accepted as a starting point. A portable Geiger counter was used for protection of nurses; areas coloured green, yellow, and red on the dosage dial indicated different levels of radiation, and corresponded to certain specified precautions which must be taken.

Concrete walls will provide protection against high-energy gamma radiation being emitted from patients, but a double layer of marble slabs 4 in. (10 cm.) thick attached to existing walls in the required area are as efficient and cheaper. Movable armour-plate screens can also be used to shield individual beds.

Personal exposure was measured by film badges for ordinary workers, or direct dosimeters for those undertaking greater risk. Extra precautions were taken when any new techniques were started. The radiation received during various procedures is given and compared with that received during ordinary radiotherapeutic or radiodiagnostic work.

Since high dosage can be given to the fingers during injections a shielded syringe holder has been devised which cuts down the radiation by a considerable factor, and does not make the syringe so heavy as to be unusable. Modifications of the apparatus for intravenous infusions have also been made so that it can be operated at a distance.

Shielding bricks are usually made from lead or cast-iron, but these are expensive and frequently give much more protection than is needed; quite often soapstone bricks, which are cheaper and very easily decontaminated, can be used.

V. M. Dalley

RADIOTHERAPY

1243. **The Radiotherapy of Pituitary Disease.** (Die Strahlenbehandlung der Hypophysenerkrankungen)
K. SCHARER. *Oncologia* [*Oncologia, Basel*] **4**, 131–166, 1951–2. 18 figs., 14 refs.

At the Roentgen Institute of the University of Zürich 99 cases of pituitary tumour have been treated with *x* rays since 1924. These cases are reported in five groups: (1) Of 35 showing no endocrine upset, histological examination in 21 showed 15 chromophobe adenomata, 2 malignant tumours, and 4 of atypical appearance; the sella was enlarged in all cases. Treatment was not uniform, and in the early years radiation dosage was too low. Comparison of a group of 13 cases treated by surgery plus irradiation with 8 treated by irradiation only showed no significant difference. The tumour dose needed is 3,500 to 7,000 r, by protracted fractionation. Of 19 adequately treated patients, 2 improved greatly and 10 were symptom-free for 1 to 12 years; the rest were either too recently treated for assessment or thought to have had cystic lesions, which are radio-resistant. *X* rays are advised as the primary treatment of choice in these cases; the visual fields should be charted regularly, and if deterioration is found, surgery can be undertaken without increased risk due to the previous irradiation. (2) Of 20 cases with endocrine changes, histology in 14 showed 7 chromophobe adenomata, and 4 malignant, 1 cystic, and 2 atypical tumours. The sella was enlarged in all cases but one. *X*-ray treatment gave good results in

10 cases for periods of 2 to 17 years. The tumour was controlled by adequate dosage, but the endocrine symptoms were hardly affected and hormone therapy was badly tolerated. Patients primarily treated surgically did no better than the others. (3) Of 28 cases with acromegaly, histology in 9 showed 4 eosinophil adenomata, 3 chromophobe adenomata, 1 cystic tumour, and 1 normal gland. The sella was enlarged in 21 cases. Adequate treatment with *x* rays alone was given in 16 cases, with great improvement in 10 for periods up to 11 years. The patient's appearance and endocrine symptoms, however, were usually unchanged. In 5 cases primary surgery and post-operative irradiation gave no better results. Early treatment is important, as slight visual changes may regress, but advanced changes are irreversible. (4) Of 14 cases of Cushing's syndrome at least 7 showed great improvement, with cure or long remission in 5. If pituitary irradiation fails, the adrenal glands may be irradiated several months later. Dosage again must be adequate. (5) In 7 cases of hypercortical syndrome (all with pseudohermaphroditism) treatment was by a variety of methods, including radiation to the pituitary and adrenal glands, but with very little success.

The general conclusion is that primary radiotherapy in adequate dosage is of greater value in all cases, with surgery later in case of failure. Good results can be expected in 80% of cases; the other 20% are mainly cases of the cystic and malignant types. *J. Walter*

1244. **The Treatment of Oral Cancer by a Combination of Radiotherapy and Surgery**

H. Wookey, C. Ash, W. K. Welsh, and R. A. Mustard. *Annals of Surgery* [*Ann. Surg.*] **134**, 529–540, Oct., 1951. 23 figs.

At the Toronto General Hospital all patients with oral cancer are seen at a combined clinic which surgeons, radiotherapists, dental surgeons, and neurosurgeons all attend. Between 1929 and 1945 there were 1,128 cases of cancer of the lip, 342 of cancer of the tongue, and 497 with lesions in other sites in the oral cavity. The average age of patients was 63 years, and from 80 to 98%, according to site of lesion, were males. It was found that cancer of the tongue affected the sides more often than the dorsum, and that remote metastases were uncommon. Oral sepsis was often a marked feature. The authors regard the histological grading of oral cancers as of doubtful value. They recognize two types, however—the keratinizing squamous type and the anaplastic carcinoma.

Response to radiotherapy was found to depend on site and accessibility more than upon histological type. Syphilis was present in 3% of the whole series (8% in cases of cancer of the tongue); this rendered treatment more difficult and results were less good. Treatment of the primary lesions was regarded as a radiological problem, except when bone was involved or in cases of residual cancer following full radiotherapy, but metastases in lymph nodes were treated by surgical dissection. Lymph-node metastases occurred in 13% of cases of cancer of the lip and 60% of cases of cancer of the tongue and other intraoral sites. Cancer of the lip was often found to invade the submaxillary nodes without invasion of deeper nodes. Intraoral lesions involved primarily the deep cervical group, with rare bizarre contralateral extensions. Prophylactic dissection was not performed for carcinoma of the lip, but was considered justifiable in growths in other sites, especially in the younger age groups. Treatment should be carried out in this order: elimination of oral sepsis; treatment of the primary lesion; treatment of metastases. Extensive but operable lymph-node metastases should, however, be treated before the primary is healed, and inoperable lesions should be treated by radiotherapy alone. Good radiation therapy needs wise clinical judgment and the application of sound physical principles. Dissection of the neck, when performed, should be radical. Removal of the sternomastoid muscle, spinal accessory nerve, and jugular vein on one side produces no disability. The external carotid artery may be sacrificed, but interference with the internal or common carotid may produce central complications. The vagus nerve on one side may also be sacrificed. Involvement of the bone of the jaw may necessitate removal of half of the mandible; this may also be necessary for radiation necrosis. Diffuse pain in advanced cases may be relieved by division of the sensory root of the 5th nerve together with division of the 2nd, 3rd, and 4th posterior cervical roots. The 9th nerve may need to be divided, and if the pain causes emotional instability prefrontal lobotomy is useful.

The results of treatment during the period under review are analysed and tabulated. For all cases of carcinoma of the lip the net and gross 5-year survival rates were 85·1% and 58·4%; of the tongue 40·1% and 33·6%; and of other intra-oral sites 37·6% and 31·8% respectively. *I. G. Williams*

1245. **Treatment of Carcinoma of the Thyroid with Special Reference to Use of Radioactive Iodine**

G. Crile. *Cleveland Clinic Quarterly* [*Cleveland Clin. Quart.*] **19**, 1–5, Jan., 1952. 1 ref.

Radioactive iodine is least effective in the undifferentiated and highly malignant types of carcinoma of the thyroid in which it is most needed. Radioactive iodine is most effective in well differentiated, colloid forming carcinomas of low malignancy, the majority of which are amenable to cure by surgical removal. The usefulness of I^{131} in the treatment of carcinoma of the thyroid is limited to the small group of carcinomas of low malignancy which have metastasized or extended beyond the scope of surgical removal. Roentgen therapy is of little value in the well differentiated carcinomas of low malignancy and should not be given prophylactically to prevent the recurrence of tumours which apparently have been excised completely.

In undifferentiated cancers of high malignancy neither operation nor treatment with radioactive iodine is of much value. Although not often effective, roentgen therapy should be given a trial.

Even the most radical operations performed within a few weeks or months of the onset of undifferentiated carcinomas of the thyroid have failed consistently to effect cures. Papillary carcinomas which are of a low

order of malignancy, and which, fortunately, are the most common type of carcinoma of the thyroid. are almost always amenable to surgical cure provided the initial operation on the thyroid is thorough and complete.

Since it is clinically impossible to distinguish between a benign, solitary adenoma and a low grade carcinoma of the thyroid, discrete adenomas should be removed completely by excising the entire lobe on the affected side. Thorough and complete removal of thyroid carcinomas and their regional metastases is the safest and most dependable treatment now available.

Inoperable recurrences or metastases of well differentiated, colloid forming cancers of the thyroid may be amenable to control by I^{131}.—[Author's summary.]

1246. ***X*-ray Treatment in Itching Skin Diseases.** (Über die Indikation zur Röntgenbestrahlung juckender Hautleiden)
F. HESS. *Strahlentherapie* [*Strahlentherapie*] **84**, 425–438, 1951. 43 refs.

A series of 147 cases of itching skin disease, among them cases of pruritus ani, lichen ruber planus, and dermatitis herpetiformis, were treated by *x*-irradiation. On the assumption that disturbances of the autonomic nervous system play a considerable part in the pathology of itching skin diseases, corresponding paravertebral ganglia were irradiated in cases of general pruritus. Usually 150 to 200 r was administered 4 times to 4 portals over the spine. Out of 10 cases 5 were completely cured and 3 considerably improved. In most cases of lichen ruber planus excellent results were obtained by paravertebral irradiation; only 1 of 12 cases thus treated did not respond. In several cases of dermatitis herpetiformis (Duhring) only temporary improvement was observed. *X*-ray treatment was most satisfactory in cases of pruritus ano-genitalis. Usually single doses of 100 r were given 3 times locally. Out of 123 patients with this complaint 50 were cured and 29 considerably relieved. It is pointed out, however, that irradiation can have no lasting improvement until toxic or psychic causes of the irritation are removed.

G. Fuchs (*Excerpta Medica*)

1247. ***X*-ray Treatment in So-called Hidroadenitis.** (Zur Röntgentherapie der sogenannten Schweissdrüsenabscesse)
G. DORNUF and H. SCHÖNWALD. *Strahlentherapie* [*Strahlentherapie*] **84**, 439–448, 1951. 1 fig.

The pathology of hidroadenitis in the armpit is discussed. The name "axillary hidroadenitis" is considered a misnomer, since the disease develops in the apocrine glands of the armpit, the secretion of which is closely linked to sex-life, and not in the true sweat glands. The incidence of the disease is highest in July and August, this being ascribed to association with increased sweat secretion during the hot season. On the basis of the experience gained in the treatment of 300 cases, it is recommended that the technique of treatment be adapted to the special conditions prevailing in each particular case. In early hidroadenitis epilation with doses of 400 to 500 r is sometimes advisable. In the presence of abscess formation or deep infiltration smaller doses of 30 to 50 r are given, by which analgesia is quickly accomplished. In the authors' opinion analgesia has definitely a favourable influence upon healing. The use of heavy dosage and higher penetration in the presence of cellulitis is not recommended. *G. Fuchs* (*Excerpta Medica*)

RADIODIAGNOSIS

1248. **Encephalography in Cerebral Atrophy.** [In English]
E. LINDGREN. *Acta Radiologica* [*Acta radiol., Stockh.*] **35**, 277–291, April, 1951. 12 figs.

The author emphasizes the difficulty of determining the degree of dilatation of the ventricular system and subarachnoid space in cases of cerebral atrophy by encephalography, particularly when carried out by operators who have little idea of the technical aspects and when only routine views are taken. The size of the normal lateral ventricle is difficult to assess, but the most accurate method is to assume that its width is one-third of the distance from its medial wall to the outer wall of the skull as seen in the antero-posterior view. Its size can vary with the amount of gas that it contains, and if the gas is unequally distributed one may appear larger than the other. The author suggests that the term "displacement" of the septum pellucidum is inaccurate as applied to the appearances in such a case, and that the term "bulging" should be used instead as its upper and lower points of fixation remain central. [This is beautifully demonstrated in the accompanying illustrations.] It can also be shown that dilatation of the ventricles may take place during the resorption of air, and as much as 7 mm. increase in width has been noted after 24 hours. The apparent size of the lateral ventricles also depends on their shape, and therefore on the type of skull. Moreover, the ventricles may be unequal in size owing to slight asymmetry of the skull, the larger ventricle being in the larger side of the skull, but on each side the ventricular width is still one-third of the distance from its medial wall to the skull wall.

These factors are all important as possible sources of error in the encephalographic diagnosis of cerebral atrophy, particularly of the general type. The more localized the change, the more easily can it generally be shown. Examples of ventricular dilatation due to local or general atrophy in conditions such as cerebral arteriovenous aneurysm (30% of such cases), general paralysis, and fracture of the skull are given and illustrated. Post-traumatic encephalographic changes consist in local or general increase in size of the lateral ventricles, widening or obliteration of the sulci on the convexity of the brain, or a combination of these changes, and finally, displacement of the ventricular system to the affected side by scarring. In general, the more severe the injury the greater the encephalographic change, but even with the most severe injuries the encephalogram may be normal in some cases.

With regard to the convexity, with good technique the various cisterns may be demonstrated in turn, and after

them the sulci, but again little is known about the normal range of size. The author emphasizes, however, that it is useless to inject a small quantity of air haphazardly, hoping that it will outline what is required, and even more so to inject large quantities, which not only causes much superimposition of the various parts of the subarachnoid space, making interpretation very difficult, but is also extremely unpleasant for the patient.

R. G. Reid

1249. **Arteriographic Demonstration of Spasm of the Intracranial Arteries. With Special Reference to Saccular Arterial Aneurisms**

A. ECKER and P. A. RIEMENSCHNEIDER. *Journal of Neurosurgery* [*J. Neurosurg.*] **8**, 660–667, Nov., 1951. 6 figs., 6 refs.

The authors describe a small series of cases of intracranial arterial spasm demonstrated by cerebral angiography, and discuss its possible significance. The intracranial portion of the internal carotid artery and its main branches were studied, and spasm was assumed to occur when the calibre of the artery was shown to be larger or smaller than in previous arteriograms performed under identical conditions. It is pointed out that pseudospasm may occur as a result of the presence of a needle in the internal carotid artery, even at some distance from the site of puncture, and that narrowing of a vessel may be also the result of arteriosclerotic changes or congenital abnormality.

In 29 cases of aneurysm demonstrated by cerebral angiography, there were 6 in which there had been a spontaneous subarachnoid haemorrhage; in all of these spasm was demonstrated according to the authors' criteria. In a further 5 there was a suggestion of spasm, but comparative films were not available. In the remaining 18 cases there was no evidence of spasm. Other conditions in which spasm was seen included post-operative narrowing of vessels following carotid ligation, post-operative astrocytoma, localized intracerebral haemorrhage and oedema, and severe intrinsic lesions of arteries.

The authors suggest that spasm following the rupture of an aneurysm may be a protective mechanism to prevent a large tear occurring, and that it may assist intra-aneurysmal thrombosis. In their cases the spasm passed off after several weeks. A common element in the production of spasm in all cases appears to be stretching of the arterial wall. *W. B. D. Maile*

1250. **The Angiographic Diagnosis of Spontaneous Thrombosis of the Internal and Common Carotid Arteries**

H. C. JOHNSON and A. E. WALKER. *Journal of Neurosurgery* [*J. Neurosurg.*] **8**, 631–659, Nov., 1951. 5 figs., 41 refs.

An account of 6 cases of spontaneous carotid thrombosis, observed at the Johns Hopkins University School of Medicine, is presented, and a further 101 cases collected from the literature are reviewed. The angiographic findings in 97 cases involved the internal carotid artery alone, the thrombosis occurring either near the bifurcation of the common carotid or at the carotid siphon. Usually a small stump was seen at the bifurcation, and angiography on the opposite side produced filling of the anterior cerebral artery, but not of the middle cerebral artery on the affected side. In 2 cases there was bilateral occlusion of the common carotid, and in a further 2 bilateral occlusion of the internal carotid. Ventriculography carried out in about half the cases showed dilatation of the ventricles on the affected side.

Suggestions as to the aetiology of the condition include thrombo-angiitis obliterans or arteriosclerosis of the vessels and retrograde thrombosis from a cerebral vessel or aneurysm. As regards treatment, cervical sympathectomy and arteriectomy have been used with little or no improvement. The condition usually presents itself in one of three forms: (1) sudden cerebral catastrophe with headache, loss of consciousness, and a rapid onset of hemiplegia; (2) slowly progressive course, characterized by severe headaches of long duration, sometimes associated with convulsive attacks, paraesthesiae, and weakness of the opposite limb; or (3) transient attacks with headaches, paraesthesiae, and hemiparesis lasting for minutes or hours and clearing up quickly or gradually. The authors suggest that routine palpation of the neck may reveal absent pulsation in the carotid, a physical sign rarely mentioned in the case histories, and that in cases in which the diagnosis is suspected, films taken should include the region of the common carotid and its bifurcations. *W. B. D. Maile*

1251. **An Experimental Evaluation of Certain Contrast Media Used for Cerebral Angiography. Electroencephalographic and Histopathological Correlations**

B. M. BLOOR, F. R. WRENN, and G. MARGOLIS. *Journal of Neurosurgery* [*J. Neurosurg.*] **8**, 585–594, Nov., 1951. 3 figs., 18 refs.

The authors, at Duke University School of Medicine, have carried out experiments to compare the effects of various contrast media on the permeability of the cerebral vessels when used for cerebral angiography. The media studied fell into 2 main chemical groups: (1) The pyridine derivatives, represented by diodone in 35%, 50%, and 70% solutions and "neoiopax", 37·5% in Ringer's solution. The non-iodinated homologues of the above substances were unobtainable, and a similar pyridine derivative, N-methylnicotinamide hydrochloride, was studied instead, in 20% solution. (2) The benzene derivatives, represented by "urokon" (3-acetylamino-2 : 4 : 6-triiodo-sodium benzoate) in 30% solution at *p*H 5·4 and 7, its non-iodinated homologue in 20% solution at *p*H 7·4, and *para*-aminohippurate in 20% solution. The experiments were carried out on adult rabbits, and a dye indicator was used to demonstrate increased vascular permeability. Electroencephalographic (EEG) recordings were obtained continuously, and the brain of each animal was examined histologically after death.

All the contrast media were found to be capable of producing abnormality in the EEG and in vascular permeability, the degree of injury varying with the amount and concentration of the medium used. The histological findings which suggested a selective toxic action of these media upon the cerebral vascular bed, were: (1) early

vasodilatation or loss of tone, which might progress to ultimate stasis; (2) severe alteration of the permeability of the blood vessels; and (3) progressive cerebral oedema as a result of the above changes. The EEG abnormalities observed paralleled the findings by the dye indicator technique and the histological changes. There was a greater tolerance for large doses when they were divided into small quantities and given at long intervals. Diodone was the least toxic of the media used. The toxic effects could be reduced by the administration of carbon dioxide. *W. B. D. Maile*

1252. **Experimental Evaluation of Cerebral Angiography**
G. A. Smith, C. M. Caudill, G. E. Moore, W. T. Peyton, and L. A. French. *Journal of Neurosurgery* [*J. Neurosurg.*] **8**, 556–563, Nov., 1951. 16 refs.

The authors have carried out, at the University of Minnesota Medical School, a series of experiments on rabbits to determine the effect of diodone in varying concentrations on cerebral vascular permeability, using as indicators dyes which stain the cerebral tissues when the blood–brain barrier is damaged. It was found that 70% diodone usually destroys this barrier and that the destruction may be accompanied by convulsions and depression of respiration, blood pressure, and pulse. When 35% diodone was used these toxic effects were much reduced. The damage did not persist for more than 3 hours, which correlates well with the reports of transient hemiplegia following cerebral angiography. The toxicity of different batches of 70% diodone appeared to vary, since with some batches no toxic changes ensued. It is suggested that the technique evolved by the authors in animals might be used to eliminate the more toxic batches. *W. B. D. Maile*

1253. **An Angiopneumographic Study of 60 Cases of Cancer of the Bronchus with Reference to Diagnosis and Assessment of Operability.** (Étude angiopneumographique de 60 cas de cancer bronchique; diagnostic, opérabilité)
A. G. Weiss and J. Witz. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **27**, 3834–3839, Dec. 26, 1951. 11 figs., 17 refs.

The authors advocate the use of angiopneumography as an aid to deciding whether a carcinoma of the bronchus is operable. They believe that the standard methods at present in use are the best means of diagnosis, being correct in 85% of cases. They point out that they have performed 225 angiopneumographies without complication. For diagnosis the pulmonary arteries and their branches provide the best evidence. In a benign tumour the vessels are pushed aside so that they seem to encircle the growth. In malignant tumours the vessels are distorted and shortened, and sometimes the branches, or even the pulmonary artery itself, may be amputated. There is a diminution in the blood supply of the corresponding part of the lung. Different histological types produce similar vascular changes. In most cases the site of obliteration of the vessels corresponds exactly with the point of stenosis of the bronchus as shown by bronchoscopy and bronchography. Similar changes may be found in advanced silicosis and in inflammatory conditions, but bronchoscopy with biopsy or aspiration will give a more precise diagnosis.

Angiopneumography shows chiefly the effect of the tumour on the intrathoracic circulation, and the appearance is often different from that seen by simple tomography or bronchography. Although exploratory thoracotomy with modern anaesthetics is relatively safe nowadays, it is better if it can be avoided. Definite contraindications to operation are metastasis or mediastinal involvement. There are unfortunately a number of patients who, although they do not show signs of these by ordinary methods, are still not operable. Detailed observation of 50 cases has enabled the authors to determine from the vascular appearances the contraindications to operation. Invasion or compression of the superior vena cava is quite common and a collateral circulation may form. Rapid injection of the opaque medium may result in over-distension of the superior vena cava with masking of the lesion. The superior vena cava is most often invaded by tumours on the right side. Sometimes there is a single indentation of the right border, at other times there is an irregular area of invasion with stasis and reflux of the medium towards the jugular veins. Changes on the left border may be due to mediastinal masses. Sometimes the whole vessel may be displaced. The passage of opaque medium may be obstructed so that filling of the right heart is very poor.

Injection of the contrast medium is best made into the right external jugular vein for tumours on the right side, and the film is taken antero-posteriorly. On the left side the left external jugular is used and the film taken in a slight left anterior oblique position. With the chambers of the heart filled one can judge the thickness of the pericardium opposite the tumour and whether it is invaded. If the pulmonary artery is cut off, the exact site in relation to the hilum must be noted. This allows the surgeon to assess the possibility of pneumonectomy; some authors hold that the left pulmonary artery must be healthy for at least 1½ cm., and the right pulmonary artery up to the bifurcation. The aorta is seldom involved, but may be displaced to the left with mediastinal involvement. No evidence as to peripheral adhesions is given by this technique.

John H. L. Conway-Hughes

1254. **Mediastinal Tumors. Angiocardiographic Study of Sixty-five Proved Cases**
C. T. Dotter and I. Steinberg. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **16**, 684–693, Dec., 1951. 7 figs., 9 refs.

The material for this paper was obtained over a period of 14 years at the New York Hospital–Cornell Medical Center, and the Medical Service of the Veterans Administration Hospital, Bronx, New York.

The authors observe that angiocardiography provides a source of information regarding displacement of thoracic structures similar to that provided by the barium-filled oesophagus; by its use the medial or inner contours of a mediastinal tumour may be delineated, whereas in other techniques these are often lost in the

homogeneous mediastinal shadow. Angiocardiography may also provide a means of estimating the effects of the tumour on cardiovascular structures; benign tumours tend to dislocate and spread the blood vessels, occasionally producing obstruction by external pressure, whereas malignant growths frequently result in irregular, sharp occlusion or invasion. Both benign and malignant conditions may be simulated by non-neoplastic conditions such as thrombosis. Differentiation from aneurysm is greatly facilitated. Comment is made on the value of the procedure to the surgeon in planning his operation and determining operability.

A histological classification is given of the 65 cases, and a number of them are illustrated by reproductions of radiographs with diagrams.

[Although this method of investigation is of considerable value in some cases of mediastinal tumour, the abstracter would not agree with the authors in predicting that it will ultimately become a routine pre-operative measure. A number of the observations in this paper have also been made by Battezzati *et al.* (*Minerva med., Torino*, 1950, **41**, 633).] *Sydney J. Hinds*

1255. **Direct and Retrograde Aortography**
R. A. DETERLING. *Surgery* [*Surgery*] **31**, 88–114, Jan., 1952. 17 figs., bibliography.

Contrast visualization of the aorta may be obtained by abdominal or thoracic aortography. In either case the injection may be made direct or by retrograde catheterization of one of the branches of the vessel. This paper is concerned principally with the technical procedures involved, and is based on 48 abdominal and 15 thoracic aortograms recorded at the College of Physicians and Surgeons, Columbia University, and the Presbyterian Hospital, New York.

The author starts by considering the contrast media which may be employed. Sodium iodide 80% was used extensively at first and produced very good contrast, but was seen to have undesirable side-effects, particularly if injected outside the vessel or if it entered the intestinal arteries. More recently iodoxyl 75% and diodone 70% have been used, with fewer and less dangerous side-effects.

For the abdominal aorta retrograde injection may be made by catheterizing the femoral artery. This method may dislodge an atheromatous plaque from the aorta and involves opening a major vessel. The author prefers the direct lumbar route of dos Santos. In this method a 16-cm., 18-gauge, malleable needle is inserted 2 cm. below the 12th rib and 7 cm. to the left of the spinous processes. The needle is pushed upwards and medially, grazes the vertebral column, and enters the aorta some 2 cm. beyond this point. The author has made 48 aortograms of this type in cases of suspected abdominal aneurysm and peripheral vascular lesions of the legs.

Direct injection of the thoracic aorta is regarded as a more hazardous procedure, perivascular haemorrhage being more frequent. For this reason retrograde injection is usually carried out. The author carried out thoracic aortography by retrograde catheterization on 15 occasions, using the left common carotid 12 times and the ulnar artery 3 times. Diodone 50%, 20 to 40 ml., was injected, and both carotid arteries were compressed during the injection. Two of the patients in whom the left common carotid was injected developed a temporary hemiplegia, and in one of the cases in which the ulnar artery was used the patient died, possibly from a dislodged atheromatous plaque.

On the whole the author does not regard thoracic aortography as a very safe procedure, and he points out that it should be used only when angiocardiography fails to give the necessary information. *D. E. Fletcher*

1256. **Axial Transverse Tomography in Surgical Disease of the Thorax.** (La stratigrafia assiale trasversa nelle affezioni chirurgiche del torace)
L. PARODI and A. ROLLANDI. *Journal International de Chirurgie du Thorax* [*J. int. Chir. Thorax*] 3, 63–104, April–June, 1951. 33 figs., 44 refs.

The authors describe the principles of axial transverse tomography and the technique introduced by Vallebona as a modification of Anusano's original method, and give details of a number of cases illustrating its usefulness in surgical thoracic disease. The technique is briefly as follows: the patient sits on a stool rotating on a vertical axis; the film is placed behind him on a horizontal carrier also pivoted on a vertical axis. These two axes are connected and can be rotated synchronously by a motor. Tube-focus, centre of plane under examination, and centre of film are arranged in one straight line. The exposure is made lasting from 1 to 2 seconds, and during this time both patient and film make one complete revolution. A 40-kW rotating-anode tube is used, with intensifying screens, and the angle of incidence is from 2 to 50 degrees. The tube–film distance is 2 to 3 metres, with 100 to 200 mA at 70 to 90 kV.

A brief description of the normal appearances in sections of the thorax at different levels is given, and 7 cases are quoted to illustrate the use of the method for the exact location of foreign bodies or tumour (includng retrosternal goitre) in the thorax, evaluation of the success of a thoracoplasty, investigation of an aortic aneurysm, and the precise location of a previously diagnosed oesophago-bronchial fistula.

The authors claim that axial transverse tomography often gives precise information as to the exact location of lesions and their relations to neighbouring structures; it is thus often invaluable in the assessment of operability. *E. L. Stein*

1257. **Indications for Barium Enema in the Diagnosis of Carcinoma of the Colon**
M. HAGGIE. *Lancet* [*Lancet*] **1**, 21–23, Jan. 5, 1952. 1 ref.

The author has reviewed the cases of carcinoma of the colon admitted to the London Hospital during the 3 years 1946–8. It was found that of 110 consecutive cases, a palpable abdominal mass was present in 51, in 35 there were signs of acute obstruction, and in 16 a growth was seen by sigmoidoscopy or felt per rectum; in only 4 cases was the diagnosis made radiologically by means of a barium enema in the absence of abnormal physical signs. Of a total of 227 barium-enema examina-

tions carried out at the same hospital during 1948, 163 showed no abnormality, and of these patients only one has since developed a carcinoma, which may have been overlooked during the examination. [This conforms closely to the figure of 25% of positive findings in barium-enema investigations, and the figure is less if one excludes minor degrees of diverticulum formation.] It is obvious, therefore, that this examination is largely used by the clinician as a means of excluding, rather than confirming, the presence of pathological changes when colon symptoms are present.

There seemed to be no great difference in the history, in many cases in this series, between patients with carcinoma and patients with nervous and functional disorders of the colon. This epitomizes the problem of selection of patients for barium-enema examination, and the author stresses the fact that rectal examination and sigmoidoscopy should always be carried out before such an examination is requested [a prerequisite for which radiologists have campaigned for many years to reduce the number of unnecessary *x*-ray investigations].

[One statement of the author's to which exception may be taken is that adequate barium-enema examination is likely to be achieved more readily after admission to hospital, it being the abstracter's experience that preparation is easier in patients who are ambulant and active. But the author rightly stresses the necessity for thorough preparation, and every radiologist will acclaim his insistence on a good history and thorough clinical examination before *x*-ray investigation.] *R. A. Kemp Harper*

1258. **Premalignant Lesions of the Gastrointestinal Tract—I. The Significance of Roentgenologic Evidence of Hypertrophic Gastritis**
R. P. BARDEN. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **66**, 915–921, Dec., 1951. 5 figs., 13 refs.

In an attempt to establish the possible relationship between chronic hypertrophic gastritis and carcinoma of the stomach the author has studied 6 cases at the Hospital of the University of Pennsylvania. [The case reports presented are scanty and the reproductions of radiographs unhelpful.] Five were in males aged 50 to 60, and the sixth in a woman aged 35. In 2 of the men a coarse rugal-fold pattern was mistaken for "carcinoma", and the partial gastrectomy specimen showed "gastritis" with no evidence of neoplasm. In one man an inoperable carcinoma of the pylorus was missed by the radiologist, who concentrated his attention on the coarse folds of the upper half of the stomach. In another man a carcinoma of the gastric antrum was correctly diagnosed from fairly typical radiographs, which showed a slight resemblance to those from one of the cases of gastritis. In the last two cases a slow-growing carcinoma was repeatedly mistaken for gastritis. From this evidence and from similar cases in the literature the author concludes that an "unpredictable number of patients with hypertrophic gastritis of several years duration will develop carcinoma. For these reasons prophylactic gastrectomy should be considered in all patients with this premalignant condition".

[There is no evidence that patients with hypertrophic gastritis are any more liable than anyone else to develop carcinoma. The difficulty is to teach diagnosis when the awkward case is so rare.] *Denys Jennings*

1259. **Some Data on the Normal Variation of the Stomach Observed Radiologically**
H. JUNGMANN and P. VENNING. *British Journal of Radiology* [*Brit. J. Radiol.*] **25**, 25–32, Jan., 1952. 2 figs., 1 ref.

In this paper the authors, who are conducting an investigation at University College, London, into the changes that may be observed radiologically in the stomach as a result of auditory and other stimuli, report on the results of preliminary work in this investigation. The observations were made on 55 healthy young adult men and women. The examination was conducted under the usual conditions for a barium-meal investigation, and was repeated on each subject 3 or 4 times at intervals of one week. The following features were studied: (1) stomach filling; (2) opening time; (3) amplitude of peristalsis; (4) rate of peristalsis; (5) rate of contractions of duodenal cap; and (6) the shape of the stomach.

The results are clearly presented with the aid of numerous tables, and show that considerable variations may occur, not only from subject to subject, but in the same subject on different occasions. The authors consider that the use of the terms "hypotonic", "orthotonic", and "hypertonic" in relation to stomach shape is unfortunate, since there is no clear relation between tonus and shape. They found that the stomach shape remained fairly constant for each individual.

[This paper is of value in helping to establish the range of normal variation of the stomach as observed radiologically, and shows that some of the signs considered to be indirect evidence of a pathological condition must be treated with reserve.] *Sydney J. Hinds*

1260. **Systematic Serial Radiography of the Biliary Tract. Technique and Preliminary Results.** (Radiographies en séries systématisées des voies biliaires. Technique et premiers résultats)
A. BUSSON. *Archives des Maladies de l'Appareil Digestif* [*Arch. Mal. Appar. dig.*] **40**, 1170–1178, Nov., 1951. 4 figs.

To visualize the biliary tract the author carries out systematic serial radiography, basing his technique on the observation that in gastrectomized patients the gall-bladder begins to empty only 5 minutes after a fatty meal, owing to the rapid arrival of the latter into the jejunum. After the patient has been for 48 hours on a fat-free diet a double dose of "pheniodol" is given, and 14 hours later serial films are taken with the patient: (*a*) erect; (*b*) supine; and (*c*) prone in a slight left anterior oblique position. In the last position the patient is given 150 ml. of iced normal saline, and 5 minutes later a fatty meal of 2 egg yolks (there being no advantage in fresh cream). Radiographs are taken at 5, 10, 15, 30, and 120 minutes.

By the author's technique the same result as is seen in gastrectomized patients is ensured: (*a*) by positioning, and (*b*) by giving iced saline, which stimulates gastric

peristalsis. The 10- and 15-minute radiographs in most cases show the gall-bladder to be half empty; it is empty at 30 minutes, and at 120 minutes is again slightly dilated at physiological rest. Further investigation in the lateral decubitus may be carried out if indicated.

The value of this technique is said to lie in: (*a*) its economy in the use of *x*-ray films; (*b*) the fact that the *x*-ray couch is occupied for only 30 minutes, the patient getting up thereafter; and (*c*) the uniformly good results obtained so long as the timing is strictly adhered to.

R. A. Kemp Harper

1261. **The Effect of Posture in Cholangiography.** (Angiocholographie et effets de posture)
J. RANTY, J. PAULHIAC, and J. CAROLI. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **28**, 203–213, Jan. 22, 1952. 14 figs., bibliography.

The authors studied the effects of posture on the biliary ducts. In their opinion the usual cholangiographs obtained in decubitus lead to erroneous conclusions, but these can be corrected by lateral radiographs—taken in profile, in decubitus, and in the Trendelenburg position, or even obtained, when this is possible, in the erect position. Manometric studies may be of help in various aspects of this problem. The reflux or flow-back into the intrahepatic ducts is not necessarily the result of hypertonicity of the canal of Oddi, but may depend upon the position in which radiographs are taken, especially as regards the right lobe.

The effect of posture upon the hepatic ducts can be rendered more evident by placing the patient in the Trendelenburg position or by accentuating lordosis by the use of an inflated balloon. By cholangiography or even by radiomanometry, in the erect position when possible, a picture of spasm of the sphincter of Oddi can be made to disappear.

The article is illustrated by numerous small radiographs and diagrams, and there is a very full bibliography.

Geo. Vilvandré

1262. **Hepatolienography: Past, Present, and Future**
S. F. THOMAS, G. W. HENRY, and H. S. KAPLAN. *Radiology* [*Radiology*] **57**, 669–684, Nov., 1951. 11 figs., bibliography.

The possible harmful effects of " thorotrast " used as a contrast medium in hepato-splenography are considered on the basis of a review of the literature and of 132 replies to a questionary addressed to radiologists. In all, there were found only 5 cases of malignant growth after the injection of thorotrast. In view of the long-standing and widespread use of this medium it may be assumed that its carcinogenetic effect in man is negligible.

More serious sequelae are the late fibrosis and scarring which may occur either in the liver or spleen or in sites of accidental extravasation of the injection. The authors are of the opinion that this possible mishap justified the condemnation of thorium dioxide as a diagnostic contrast medium for hepato-splenography. They define the ideal contrast medium and analyse the various alternative media, old and new. They suggest that, as iodized and brominated fatty acids have to be given in large quantities, they may produce allergic or toxic reactions in predisposed individuals. Colloidal suspensions of non-toxic metals, such as tantalum, have proved sufficiently radio-opaque and harmless to justify further experimentation. Satisfactory opacification of the liver and spleen has been obtained with emulsions of iodized or brominated oils, given either by the mouth or by injection, but these media, too, are still under investigation. *A. Orley*

1263. **Pneumopyelography**
J. S. RITTER and W. H. SHEHADI. *Urologic and Cutaneous Review* [*Urol. cutan. Rev.*] **55**, 649–652, Nov., 1951. 8 figs., 4 refs.

In this paper from New York the use of air for outlining the renal pelvis—pneumopyelography—is described. The most valuable application of this method is said to be in the demonstration of non-opaque renal calculi, whose presence could not be demonstrated by the routine methods of pyelography. Three case histories are given and radiographs reproduced to illustrate this particular use. It is claimed that the method is free from danger, and that the best results are obtained by using a special ureteric catheter carrying a small inflatable bag near its tip by which the pelvis can be shut off while air is injected into it. *F. B. Cockett*

1264. **Retropneumoperitoneum and its Value in the Study of the Adrenal Glands.** (Sur le rétropneumopéritoine et son importance dans l'étude des capsules surrénales)
E. COELHO, J. M. DA FONSECA, A. NUNES, and R. PINTO. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **27**, 3840–3844, Dec. 26, 1951. 10 figs.

The authors detail the difficulties of technique of pneumoperitoneum and perirenal insufflation and cite some of the complications which have prevented these procedures from coming into general use. In 1948 Rivas of Madrid introduced the technique of retropneumoperitoneum with which this paper is concerned. The technique is easy, the procedure harmless to the patient, and it gives excellent radiographic visualization. The subserous tissues of the body have a remarkable anatomical continuity; the tissue in front of the sacrum and surrounding the pelvic organs is in continuity with that between the parietal peritoneum and the abdominal wall; it then penetrates the diaphragm at numerous points, and is in continuity with the mediastinal and cervical tissues, surrounds the coats of the great vessels and nerves, and connects with the cellular tissue of the limbs.

Retropneumoperitoneum is especially useful in demonstrating the renal shadows and the adrenal glands. The patient is placed in the genu-pectoral position and the sacro-coccygeal joint identified; the injection is made 1 or 2 cm. to one or other side. The skin is anaesthetized and a lumbar puncture needle introduced forwards, inwards, and upwards, so as to lie parallel with the anterior wall of the sacrum. Aspiration with a syringe is carried out to make certain a vessel has not been punctured. A little air is then introduced and the needle positioned until there is no resistance. A pneumothorax apparatus connected to an oxygen cylinder, fitted with a meter to measure the pressure and

volume of gas introduced, is used. Not more than 1,200 to 1,500 ml. of oxygen is used. The oxygen is introduced under screening control. Radiographs, usually one in the supine position and one erect, are taken; for the adrenal glands oblique radiographs are most useful. Tomography and compression is also made use of by the authors to help visualization. In only one case was a slight perineal emphysema produced. Accidental puncture of the rectum should be avoided. Some patients complained of a fullness in the lumbar region and pain in the shoulders, but this was of no importance. Four to 5 hours after injection the gas commences to disperse, and in 24 hours is only in the retroperitoneal space. Among the cases described are 7 cases of Addison's disease, 3 of Cushing's syndrome, 2 of acromegaly, and several cases of hypertension. Some of these are illustrated.

John H. L. Conway-Hughes

1265. **A Radiological Contribution to the Problem of Nephroptosis.** (Röntgenologischer Beitrag zum Problem der Wanderniere)

G. LIEB. *Zentralblatt für Chirurgie* [*Zbl. Chir.*] **76**, 1654–1660, 1951. 7 figs., 6 refs.

As is well known, the indications for operation on a movable kidney have undergone considerable modification during the last 50 years, and there is some danger that the pendulum may have swung too far in the direction of dismissing all such cases as manifestations of a neurosis. The present paper suggests that diagnosis may be put on an exact footing by a planned series of radiographs taken lying and standing.

A ureteric catheter is inserted after cystoscopic examination, and the renal pelvis filled with contrast medium under direct *x*-ray control. A series of exposures are made of the kidney and ureter at various stages of the filling and from different angles. Before making the last of these exposures the catheter is slightly withdrawn from the pelvis and the apparatus adjusted to demonstrate any alteration in the lower calices, and especially to visualize correctly the origin of the ureter from the pelvis. At the conclusion of the examination one or more exposures are made with the patient standing. This routine has been standard at the St. Jacob Hospital, Leipzig, since early 1949. By September of that year, out of 230 pyelograms from patients suspected of kidney disease, 25 showed definite nephroptosis; most of these cases were thought originally to be cases of renal or ureteric calculus. By the method described, the outward tilting of the axis of a ptosed kidney depending from its pedicle and dragging upon it, with the production of colicky attacks of true pedicle pain, can be visualized. The characteristic "faded carnation" appearance shown on the *x*-ray plate, taken in conjunction with the syndrome associated with pedicle pain, forms the surest indication for nephropexy.

It is of considerable importance to know before operation whether a dilatation seen in the renal pelvis, caused by urinary retention due either to kinking of the ureter against a dropped kidney or to an aberrant renal artery, is an irreparable hydronephrosis or whether it is merely a mechanically produced enlargement, in the prehydronephrotic stage, which is likely to be cured by removal of the cause of the constriction. This question may be settled by observing whether in the serial radiographs the normal constrictor reflex, which empties the kidney pelvis in the standing position, is present or not.

D. P. McDonald

1266. **Dynamic Phlebography**

J. A. FERREIRA, E. J. F. VILLAMIL, and A. O. CIRUZZI. *Angiology* [*Angiology*] **2**, 350–373, Oct., 1951. 19 figs., 26 refs.

In the investigation by phlebography of the veins of the lower limb, the injection of contrast medium in the retrograde direction has the merit of demonstrating the competence or incompetence of the valvular system. To obviate the need to expose the femoral vein, Roche Robertson *et al.* (*J. int. Coll. Surg.*, 1949, **12**, 516) developed a technique whereby a ureteric catheter is introduced into the lesser saphenous vein in the upper part of the calf and passed upwards 15 cm. to enter the femoral vein, and the injection made as the patient is brought into the upright position on a tilting table. The present authors describe their modification of this procedure, the chief points of difference being that: (1) a special cassette-changer is used to enable two exposures to be made in rapid succession; (2) plastic tubing is substituted for the ureteric catheter to allow of more rapid injection, and is inserted only 2 cm. into the vein to avoid penetration of the superficial venous system; (3) the patient remains prone throughout; and (4) the angle of tilt is limited to 45 degrees, at which point the injection (20 ml.) is made; radiographs of the upper and lower leg are then taken immediately, and two further radiographs after the muscles of the leg have been contracted vigorously for a few minutes. Various types of appearance observed in a series of 150 cases are described and illustrated.

In normal subjects retrograde filling of the vein stops at the first valve distal to the site of entry, and little contrast medium is seen below the level of the knee-joint. Incompetence of the deep veins leading to backflow is of two main recognizable types—that due to inadequacy of the valves (described as "essential" or "idiopathic"), and that due to a post-thrombotic state. Radiologically, the former is recognized by smooth filling of the veins, which show bulges at the site of the incompetent valves. In the latter condition the filling is less regular and, more characteristically, the site of the valves cannot be seen. Valuable evidence of the presence of incompetent communicating veins may be provided by retrograde filling of the superficial groups, usually best shown in the films made after muscular contraction. The clinical aspects are very briefly discussed.

A. M. Rackow

1267. **Soft Tissue Radiography. Technical Aspects and Clinical Applications in the Examination of Limbs.** [In English]

A. FRANTZELL. *Acta Radiologica* [*Acta radiol., Stockh.*] Suppl. 85, 1–103, 1951. 37 figs., bibliography.

Paediatrics

1268. **Influence of Diet on the Occurrence of Hyperphosphatemia and Hypocalcemia in the Newborn Infant**
I. F. GITTLEMAN and J. B. PINCUS. *Pediatrics* [*Pediatrics*] **8**, 778–787, Dec., 1951. 8 figs., 16 refs.

The effect of various diets containing different amounts of vitamin D on the serum calcium and phosphorus levels of newborn infants was studied by the authors at the Jewish Hospital of Brooklyn, their findings confirming those of previous workers. The diets studied were: evaporated milk, breast milk, diluted cow's milk, and diluted cow's milk with added vitamin D. Blood was obtained from the femoral vein for the estimation of serum calcium and phosphorus levels by the ultramicrochemical method of Sobel in infants of different age groups fed on each diet. There were as many as 253 infants in the group given evaporated milk, but in the other groups the numbers were smaller. Statistical analysis of the results shows that in infants fed on evaporated milk, and to a lesser extent in those fed on cow's milk, there was a tendency to develop hypocalcaemia and hyperphosphataemia, whereas on breast milk normal levels were maintained. The addition of vitamin D to cow's milk seemed to accentuate this tendency. Although several factors play a part in the hypocalcaemia of the newborn infant, emphasis is placed on the fact that in breast milk the total phosphate content is only one-seventh, and the inorganic phosphate content only one-thirteenth, of that of cow's milk.

David Morris

1269. **Neonatal Surgery. Early Treatment of Congenital Malformation**
P. P. RICKHAM. *Lancet* [*Lancet*] **1**, 332–339, Feb. 16, 1952. Bibliography.

A statistical review of congenital malformations as a cause of neonatal mortality is given. Attention is drawn to the high mortality (61%) following surgical treatment. The establishment of regional centres where expert treatment could be given is suggested as a possible way of reducing the mortality.

In the Liverpool region in 1949, 75 cases of congenital malformation accounted for 16·44% of all neonatal deaths, a large proportion (54 cases) of which were due to conditions amenable to surgery. The incidence is given as follows: duodenal atresia 5; small-bowel obstruction, extrinsic 7, intrinsic 3; neonatal peritonitis 5; meconium ileus 1; Hirschsprung's disease 1; strangulated hernia 1; oesophageal atresia 8; imperforate anus 8; exomphalos 7; atresia of the biliary passages 6; diaphragmatic hernia 4; genito-urinary 2; suppurative parotitis 2; spina bifida 7; and miscellaneous 8. Similar figures for the Hospital for Sick Children, Great Ormond Street, London, are quoted for comparison. Some points in the diagnosis of these conditions are mentioned. Of 54 patients operated on 33 died, an operative mortality of 61%. The principal causes of death were shock, peritonitis, intestinal obstruction, respiratory complications, and enteritis. Congenital pyloric stenosis was excluded from the review because the recognition and present surgical treatment of the condition were considered satisfactory. The social status, age, and diseases during pregnancy of the mothers, and the order of birth, seasonal incidence, and heredity are discussed as aetiological factors.

Charles P. Nicholas

1270. **Mercury as a Cause of Pink Disease**
G. A. JAMES. *Great Ormond Street Journal* [*Gt Ormond Str. J.*] No. 1, 48–51, June, 1951. 5 refs.

As it has recently been suggested that ingestion of mercury may be a cause of pink disease, the author has investigated the mercury content of the urine in 6 cases of that disease, 5 patients with some, but not all, of the features of the disease, and 16 children to serve as controls. Controls were mainly unselected, but some effort was made to include both children who were teething and those who were not, bearing in mind that the most popular brands of teething powders contain mercury subchloride.

In the 6 cases of pink disease the mercury content of the urine ranged from 51 to 530 μg. per litre (average 218·5 μg.); in the atypical cases, from 64 to 710 μg. per litre (average 366·8 μg.); and in the controls, from 0 to 380 μg. per litre (average 73·1 μg.).

The author suggests that atypical cases of pink disease may be due to chronic mercury intoxication, whereas for true pink disease an additional element of hypersensitivity to mercury is necessary. He concludes from his findings that as regards the ingestion of mercury as an aetiological factor in pink disease the case is " not proven ".

M. MacGregor

1271. **Treatment of Dehydration in Infancy Using Continuous Interstitials and Hyaluronidase**
A. M. GOODFELLOW, R. POCOCK, and J. F. MCCREARY. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **66**, 8–11, Jan., 1952. 1 fig., 12 refs.

In this paper from the University of Toronto the treatment of dehydration in infancy by interstitial administration of fluid combined with hyaluronidase is discussed. Concerning technique it is suggested that the antero-lateral and lateral aspects of the thighs are the most satisfactory sites for the injection. The drip apparatus is filled with appropriate fluid, usually two parts of 5% glucose to one part of normal saline; this may be supplemented with Ringer's lactate. An ampoule of " wydase " (frozen dried hyaluronidase) is dissolved in 1 ml. normal saline, and 0·5 ml. injected into the tube running to each thigh. Thus the hyaluronidase is carried to the tissues in the first flush of the fluid.

Of 24 cases so treated, in 4 the patient was so severely dehydrated that the intravenous route had to be used for the first 24 hours, hydration being thereafter maintained interstitially.

Tables of biochemical analysis are given to show the effectiveness of this method of rehydration. The importance of sterility and maintenance of dry and clean dressings is stressed; with these precautions infection was not encountered. Sensitivity to hyaluronidase was tested in 50 infants, but in none of them was a typically positive result obtained.

The advantages of this method of treating dehydration are considered to be the ease of technical administration and observation—factors which are particularly useful in small hospitals. *A. T. MacQueen*

1272. **Scurvy in Mentally Defective Children**
D. W. BEYNON and P. R. EVANS. *Great Ormond Street Journal* [*Gt Ormond Str. J.*] No. 2, 90–98, Dec., 1951. 5 figs., 6 refs.

During a period of 2½ years ending in December, 1949, only 10 children suffering from scurvy were seen at the Hospital for Sick Children, Great Ormond Street, London, of whom 6 were mentally defective, nearly all being over 2 years of age. Full notes of these 6 cases are given. The later onset of symptoms than is seen in infantile scurvy is accounted for by the fact that all these patients had been breast-fed and it was only later that difficulties in feeding had arisen associated with the mental condition. All the children had cut teeth, and the obvious gum changes led to the diagnosis. The misery of the child and the extreme tenderness of the limbs were prominent symptoms, associated with loss of appetite and weight, and in 2 cases with follicular keratosis. In 2 cases haemorrhages had occurred, in one causing subcutaneous bruising, and in the other a subperiosteal haematoma of the femur. An interesting phenomenon occurred in 3 children with spastic diplegia. With the onset of scorbutic symptoms their legs, which had previously been immobile in extension, became flexed against the abdominal wall, all attempts at extension causing pain. Extension of the limbs again became possible after treatment of the scurvy.

There was no evidence of rickets, and anaemia was not a marked feature. Radiographs of the long bones showed definite evidence of scurvy in 1 case, early scorbutic changes in 3, and no evidence of scurvy in 2. Estimation of the urinary ascorbic acid content and saturation tests were useful in confirming the diagnosis. The cases responded rapidly to 500 mg. of ascorbic acid given daily by intramuscular injection. *H. S. Stannus*

1273. **Heredity, Maternal Age, and Birth Order in the Etiology of Celiac Disease**
M. W. THOMPSON. *American Journal of Human Genetics* [*Amer. J. hum. Genet.*] 3, 159–166, June, 1951. 29 refs.

In this paper details of the birth order, maternal age, and familial distribution of 119 patients with coeliac disease are presented. The birth rank of affected children was found to be significantly lower than for their normal sibs. Similarly the average maternal age at the birth of affected children was significantly higher than in the case of their normal sibs. The disease also occurred more frequently among the sibs and other relatives than might have been expected on a chance basis. These findings are taken to indicate that the unfavourable uterine environment of older and multiparous mothers may be important in bringing about the manifestation of coeliac disease in a child genetically predisposed. *Harry Harris*

1274. **Study on Etiology, Epidemiology, and Antibiotic Therapy of Infantile Diarrhea, with Particular Reference to Certain Serotypes of *Escherichia coli***
E. NETER, C. R. WEBB, C. N. SHUMWAY, and M. R. MURDOCK. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **41**, 1490–1496, Dec., 1951. 22 refs.

Two serotypes of *Bacterium coli*—0111 (D433) and 055—were isolated from 14 cases of infantile diarrhoea, and in 11 instances also from nasopharynx and throat, which suggested an air-borne infection. These strains were not encountered among 608 strains of *Bact. coli* isolated from the faeces of infants not suffering from gastro-enteritis or from various sources in adults. In tests *in vitro* both serotypes proved to be highly sensitive to aureomycin, chloramphenicol, and terramycin; distinctly less sensitive to streptomycin; and resistant to penicillin and bacitracin. Aureomycin was given by mouth in a dosage of 50 to 70 mg. per kg. body weight per 24 hours; terramycin by mouth in a dosage of 60 to 70 mg.; and chloramphenicol intramuscularly in a dosage of 35 to 150 mg. per kg. body weight. Clinical improvement resulted within 3 to 4 days, and the suspected strains were eliminated in all but one case (treated with chloramphenicol in high dosage), in which the numbers of the organisms were greatly reduced.

The authors recommend isolating sporadic cases in order to avoid cross-infection, especially in hospital.
R. Salm

1275. **Volvulus of the Greater Curvature of the Stomach as a Cause of Vomiting in Infancy.** (Plicatura de la gran curvadura del estomago como causa de vomito en el lactante)
A. DOBERTI, J. E. HOWARD, W. BUSTAMANTE, and A. WINTER. *Revista Chilena de Pediatria* [*Rev. chil. Pediat.*] **22**, 409–414, Oct., 1951. 4 figs., 6 refs.

Partial or total volvulus of the greater curve of the stomach was found in 12 infants in a period of 2 years at one Chilean hospital, and it may be more common than is at present thought. Symptoms of vomiting or regurgitation developed at birth or up to the age of 13 weeks; there were no particular features about these symptoms. Radiological examination is considered essential if the diagnosis is to be made, since pylorospasm or habit vomiting is simulated.

Radiographs showed that the stomach appears like an elongated "S" in the incomplete variety, but when volvulus is complete it tends to be kidney-shaped. Factors considered of aetiological importance included gaseous distension of the colon, which then ascends and tends to rotate the stomach, laxity of the supporting

structures of the stomach in the newborn, and organic defects. The only fatal case was found to have hypertrophy of the pylorus. Treatment is by small frequent feeds and by posture, but details are not given. Surgery may occasionally be required. *K. Gurling*

1276. **Potassium Deficiency in Entero-colitis in Infancy: its Clinical Features, Treatment and Prevention**
H. WILLIAMS. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 313–317, March 8, 1952. 10 refs.

1277. **Idiopathic Thrombopenic Purpura in Childhood**
W. A. NEWTON and W. W. ZUELZER. *New England Journal of Medicine* [*New Engl. J. Med.*] **245**, 879–885, Dec. 6, 1951. 5 figs., 14 refs.

The authors discuss the natural history of idiopathic thrombopenic purpura as seen in 47 children between the ages of 9 days and 7 years, the majority of whom were followed for a significant period of time. Children between the ages of 2 and 8 years were the most frequently affected. The diagnosis was based on a platelet count of less than 100,000 per c.mm. associated with clinical evidence of an abnormal bleeding tendency.

There were 28 boys and 19 girls, 41 of whom were white and 6 negroes. No relation to antecedent infection or allergy was demonstrated, but there was a suggestive tendency towards a seasonal incidence, with a peak in the spring. There was an impressive family history of bleeding in only one case. In 29 of 42 cases observed for 6 months or more bleeding ceased within a month; in the others it lasted for longer periods up to 3 years. Bleeding occurred into the skin in 46 cases, into the oral and conjunctival mucous membranes in 21, from the nose in 15, from the urinary tract in 5, from the gastro-intestinal tract in 4, from the vagina in one, and into the nervous system in 4 (2 of which were regarded as due to haemorrhagic encephalitis) Definite splenomegaly was found in one case, though the tip of the spleen was palpated in 5 others. Marrow biopsy showed no consistent abnormalities, either in the number of megakaryocytes or in the degree of eosinophilia present, and was of no assistance in prognosis. It was of value, however, in excluding other primary diseases.

Blood transfusions were given to 27 patients, and splenectomy was performed on 7, of whom one died. Of 40 patients treated conservatively, 2 died within a few days of the onset. Adequate criteria for splenectomy were not established. *John D. Hay*

1278. **Congenital Lobar Emphysema**
R. ROBERTSON and E. S. JAMES. *Pediatrics* [*Pediatrics*] **8**, 795–804, Dec., 1951. 10 figs., 8 refs.

Congenital lobar emphysema, a condition which has received scant attention in the past, is well illustrated by 5 new cases reported from the Vancouver General Hospital. In all 5 there was intermittent cyanosis and dyspnoea, and clinical evidence of obstructive emphysema was confirmed by *x* rays. In 3 cases lobectomy was successfully performed, but the other 2 infants died before surgical treatment was attempted. The cause of the condition is thought to be bronchial obstruction due to either a congenital valve or a mucosal fold, and this view is supported by the Jacksons' bronchoscopic findings. The differential diagnosis is discussed and emphasis placed on the need for more frequent recognition of the condition, as early diagnosis and surgical treatment produce excellent results in what is otherwise a fatal condition. A brief description is given of 3 similar, previously reported, cases. *David Morris*

1279. **Perianal Dermatitis of the Newborn**
A. G. PRATT. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **82**, 429–432, Oct., 1951. 1 fig., 12 refs.

Perianal dermatitis of the newborn is well recognized by paediatricians, although in standard textbooks, and too often in practice, it is not differentiated from ammoniacal dermatitis of the napkin area. The incidence was higher among babies artificially fed than those breast-fed in a group of 1,100 studied at the Cooper Hospital, Camden, New Jersey. This included a group of negro babies, who were less frequently affected. As the condition is thought to be due to the alkalinity of the stools, 253 babies having artificial feeds were given lactose in place of dextrimaltose to make the stools less alkaline. The incidence fell from 35·3% to 23·7%, but statistical analysis showed this to be hardly significant.
David Morris

1280. **Transient Synovitis of the Hip Joint in Children. Report of Thirteen Cases**
E. G. EDWARDS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 30–34, Jan. 5, 1952. 6 refs.

The author describes 13 cases of transient arthritis of the hip. Transient arthritis or transient synovitis is a well-recognized clinical condition occurring in a child between the ages of 5 and 10, with pain in the hip and a limp. Movements of the hip are restricted, but the radiograph is normal. The symptoms and signs disappear after a few days' rest in bed. The cause of the malady is not known. Its interest lies in the difficulty encountered in differentiating it from more serious diseases of the hip. *George Perkins*

1281. **Congenital Duodenal Obstruction and Mongolism**
M. BODIAN, L. L. R. WHITE, C. O. CARTER, and J. H. LOUW. *British Medical Journal* [*Brit. med. J.*] **1**, 77–78, Jan. 12, 1952. 7 refs.

In a consecutive series of 32 infants with congenital atresia or stenosis of the duodenum a high incidence of mongolism was observed.

The frequency of this association has not been generally appreciated, presumably because most children with duodenal atresia or stenosis die during the neonatal period, when mongolism is apt to be overlooked. The features of the newborn mongol are therefore reiterated. It is felt that the early recognition of mongolism in a newborn child with suspected duodenal obstruction may be of practical importance in the management of the case.—[Authors' summary.]

Medicine: General

1282. **Lycopodium Allergy.** [In English]
E. B. SALEN. *Acta Allergologica* [*Acta allerg., Kbh.*] **4**, 308–319, 1951. 2 figs., 16 refs.

Lycopodium is the name given to the spores of the moss *Lycopodium clavatum*. This is found in damp woodlands and is used for Christmas decorations in Sweden, in which country it spores in July and August. Lycopodium powder is used in certain industries and professions, and those who handle it may become sensitive to it. Thus cases of allergic rhinitis or asthma have been reported in theatre personnel, in pharmacists, in workers in certain metals and in the fireworks industry, and in hairdressers. A case of lycopodium sensitivity is reported in a boy whose symptoms had an environmental incidence and a tendency to occur in late summer, and whose only positive skin reaction was to lycopodium.

A. W. Frankland

1283. **Phenergan: a Clinical Evaluation. Based on a Study of 193 Allergic Patients**
M. M. PESHKIN, H. G. RAPAPORT, and S. GROSBERG. *Annals of Allergy* [*Ann. Allergy*] **9**, 727–740, Nov.–Dec., 1951. 18 refs.

" Phenergan " (promethazine) was given to 71 children and 122 adults with allergic conditions, usually 25 mg. orally for periods up to 300 days. The response was best in urticaria and angioneurotic oedema and poor in asthma, eczema, and neurodermatitis. [The latter is not surprising in view of the small dosage.] The drug proved more efficacious than any other antihistaminic. No harmful effects on the blood and blood-forming organs could be detected. *H. Herxheimer*

1284. **Allergic Dermal-respiratory Syndrome in Children**
B. RATNER, C. COLLINS-WILLIAMS, and S. UNTRACHT. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **82**, 666–676, Dec., 1951. 2 figs., 37 refs.

The authors studied a series of 750 children with dermal (urticaria, eczema) and respiratory (perennial rhinorrhoea, hay-fever, asthma) manifestations of allergy. Of the total, 109 were seen in infancy, 198 between the ages of 2 and 5 years, and 265 between the ages of 5 and 10. The ratio of boys to girls was 1·5 to 1. Both dermal and respiratory evidence of allergy was found in 35%, respiratory symptoms only in 41%, dermal syndromes only in 22%, and other allergic syndromes in 2%. Eczema with asthma was by far the commonest form of combined allergy; 59% of all patients with eczema or a history of eczema developed respiratory allergy. Eczema almost always began during the first year of life. The onset of asthma was most commonly at the age of 3 to 4 years, and of hay-fever by the sixth or seventh year.

Observation of a series of cases of dermal allergy together with repeated skin tests showed the following to be the stages in the development of dermal respiratory allergy. Stage 1.—Dermal allergy alone is present; positive skin reactions are obtained to foods but not to inhalants. Stage 2.—Either there is sensitivity to inhalants as determined by skin tests, without evidence of respiratory allergy; or there is respiratory allergy but the reaction to skin tests with inhalants is negative. Stage 3.—Both dermal allergy and respiratory allergy are present and the results of skin tests to inhalants are positive. As would be expected, the cases at Stage 1 are mostly in infants, with the proportion of cases in older children rising as Stage 3 is reached.

The authors believe that thorough treatment will prevent the development of respiratory allergy in children with allergic dermatitis. They advise the use of denatured food in cases of eczema, with symptomatic treatment of the dermal lesions. Foods giving positive reactions are removed from the diet and contact with inhalants is avoided. The child is immunized by subcutaneous injection of extracts of all foods and inhalants giving positive reactions. Skin tests are repeated annually to discover fresh sensitivities Attention is drawn to the value of examination of the nasal smear as a means of differentiating between infective and allergic conditions of the nose.

[The treatment recommended is perhaps over-idealistic and does not take into consideration the non-allergic factors, particularly emotional influences, which may be of considerable, and sometimes primary, importance. It might be thought that courses of injections with agents not known with certainty to be the cause of symptoms would have serious disadvantages in young children.]

R. S. Bruce Pearson

1285. **A Statistical Study of 400 Cases of Allergic Bronchial Asthma.** (Quatre cents cas d'asthme bronchique allergique. Étude statistique)
P. VALLERY-RADOT and P. BLAMOUTIER. *Presse Médicale* [*Pr. méd.*] **59**, 1697–1698, Dec. 22, 1951.

Scratch-test reactions in 400 cases of non-infective allergic asthma were positive in 212 cases to one allergen only, and in the remaining 188 cases showed multiple sensitivity. Of the 198 patients who gave positive reactions to house dust, 34 reacted to no other test substance, the others reacting also to various other allergens. Next to house dust, feathers produced the greatest number (192) of positive reactions, 55 patients reacting to this allergen only. Amongst other allergens to which positive reactions were obtained were animal hairs (99 cases), wool (33), silk (4), cotton (2), kapok (2), industrial allergens such as flour (17), dyes (4), and sawdust (3), food allergens (17), and drugs (18). Pollen sensitivity was found in 40 cases, 26 patients reacting to pollens only. Mould tests gave only 8 positive reactions, but the authors suggest that intradermal tests may give more. [Intradermal testing of house-dust-sensitive

patients with mould extracts by the abstracter gave positive reactions in 55%.]

In the authors' experience most patients with allergic asthma are under 35 years old, and only an occasional patient over 50 is seen with infective asthma associated with dust and feather sensitivity. *J. Pepys*

1286. **Subcutaneous Implantation of Pellets of *iso*Propylnoradrenaline (Isuprel) in Cases of Bronchial Asthma.** (Implantes subcutaneos de pellas de isopropilarterenol (Isuprel) en enfermos de asma bronquial)
J. LEWIN, A. MERY, and F. HUIDOBRO. *Revista Médica de Chile* [*Rev. méd. Chile*] **76**, 741–745, Dec., 1951. 2 figs., 11 refs.

Subcutaneous implantation of pellets of *iso*propylnoradrenaline (isoprenaline) stearate has been carried out 18 times in 15 patients with well-established bronchial asthma. The isoprenaline was in the form of the stearate and was mixed with an equal quantity of cholesterol to delay absorption, the dose varying from 78 to 667 mg. of isoprenaline base. The first implantations were considered too small and in the majority of cases the dose was over 450 mg. of the base.

There was excellent improvement in 6 patients, who became free of symptoms; in 2 the result was good in that no other treatment was necessary, though a slight element of asthma persisted; in 7 the effect was satisfactory, drugs being required less frequently than before the implantation and the asthma less troublesome; while 3 patients were not benefited, but in 2 of these cases the dose was probably too small. Good effects were apparent 10 hours after insertion and were greatest 7 to 10 days later, lasting on the average about 40 days. The asthma was reduced in severity for as long as 9 months in some instances. No generalized toxic effects are reported, but local pain, swelling, and redness are to be expected. *K. Gurling*

1287. **The Treatment of Bronchial Asthma with Nitrogen Mustard.** (Tratamiento del asma bronquial por medio de la mostaza nitrogenada)
L. HERRÁIZ BALLESTERO and C. RODRÍGUEZ FONTELA. *Prensa Médica Argentina* [*Prensa méd. argent.*] **38**, 3063–3072, Nov. 23, 1951. 17 refs.

Treatment with nitrogen mustard was given to 19 patients with long-standing bronchial asthma who had failed to respond to the usual treatments, and who had been wheezing for over one week. The dose of methyl-tris-(β-chlorethyl)-amine hydrochloride was 1 mg. per 10 kg. body weight, though the first injection was usually limited to a total of 3 mg., and subsequently to 6 mg. An intravenous drip was set up to minimize local reactions. The usual toxic symptoms of nausea, vomiting, and leucopenia were noted. Of the 19 patients 12 had a total remission of symptoms, 3 were partially relieved, and in 4 there was no benefit. In some cases the asthma was initially worse but relief followed within a few hours if any was to be obtained, and the vital capacity also increased at the same time. The minute volume was also increased, the leucocyte count fell, but the eosinophil counts varied. Remissions lasted under 1 week in 4 cases, between 4 and 5 weeks in 4, and over 5 weeks in 6.

In the 4 patients deriving no benefit, vomiting, tachycardia, and diminution in the vital capacity limited treatment, and the leucocyte count tended to fall less than in the other cases. *K. Gurling*

1288. **Oral Cortisone Therapy in Intractable Bronchial Asthma**
E. SCHWARTZ. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1734–1737, Dec. 29, 1951. 1 fig., 7 refs.

In a study in New York 22 patients with chronic intractable bronchial asthma have been treated with orally administered cortisone. The ages of the patients varied between 5 and 67 years, and the asthma had been present for from 4 months to 35 years. Before cortisone therapy was begun these patients had had " moderately severe or very severe asthmatic attacks ranging in duration from 4 days to 6 years, and were resistant to all other forms of therapy ".

During treatment with cortisone a daily record was kept of the patients' weight, fluid intake and output, blood pressure, and urine tests for sugar. The adult dose of cortisone varied between 200 and 300 mg. on the 1st day, 100 to 200 mg. on the 2nd day, and 100 mg. on subsequent days until adequate relief was obtained; the dose was then reduced to the minimum amount necessary to maintain relief. The average maintenance dose was 25 mg. twice daily. The duration of therapy ranged from 1 to 45 days, and children received from 25 to 75% of the adult dose.

The asthma was " definitely relieved " in 26 of 31 courses of treatment given to 22 patients. In 5 patients, 4 of whom had emphysema, no benefit was obtained. Improvement began in less than 12 hours in 18 patients, in 24 hours in 6, in 48 hours in one, and in 72 hours in one. Improvement was maintained as long as treatment was continued. In 18 patients relapse occurred within 2 weeks after cortisone therapy was stopped. The shortest remission was for 12 hours, the longest 210 days. There was no correlation between the total dosage or the duration of therapy and the length of the remission. One patient died suddenly after 2 days of cortisone therapy, from heart failure during an acute attack of asthma.

It is pointed out that cortisone therapy is not a substitute for allergic therapy. *R. S. Bruce Pearson*

1289. **Intravenous ACTH Therapy in the Treatment of Bronchial Asthma**
M. S. SEGAL and J. A. HERSCHFUS. *Diseases of the Chest* [*Dis. Chest*] **20**, 575–587, Dec., 1951. 8 refs.

Intravenous ACTH therapy was given at the Boston City Hospital to 10 patients with bronchial asthma, 10 mg. being added to each litre of a 5% solution of glucose. Of this preparation, 3 litres, containing 30 mg. ACTH, was infused in the first 24 hours. As improvement occurred the dose was reduced to 10 or 15 mg. of ACTH daily. The total administered ranged from 10 to 210 mg. in periods up to 9 days. Relapse followed within a short

period in 2 of the 7 patients whose symptoms disappeared, and in the other 3 there was a certain degree of improvement. No patients failed to obtain some relief, although the follow-up period was short (from 1 to 8 weeks only).

The authors claim that, as compared with intramuscular injection, intravenous therapy is cheaper; it is also more effective, since in at least one case relief was obtained, with fall in eosinophil count, after intramuscular treatment had failed. No allergic reactions were noted. It is pointed out that when treatment is terminated fever and bronchitis may follow, and for this reason concomitant antibiotic therapy is recommended.

K. Gurling

1290. **Hospital and Ambulatory Treatment of Asthma and Eczema with ACTH and Cortisone**
H. S. BALDWIN and P. F. DEGARA. *Journal of Allergy* [*J. Allergy*] **23**, 15–26, Jan., 1952. 13 refs.

At the New York Hospital–Cornell Medical Center 11 patients with a long history of chronic asthma, and 8 patients with severe atopic eczema, were treated with, usually, 100 mg. of cortisone per day in the case of asthma and 70 mg. in the case of eczema. All patients except one asthmatic had satisfactory relief while in hospital. In one patient lung function studies were carried out, and these showed improvement. In 9 asthmatics and 5 patients with eczema the treatment was continued after discharge from hospital; the former received 75 to 100 mg. and the latter 40 to 80 mg. of cortisone. Only 3 asthmatic patients and one with eczema were able to discontinue taking the hormone, although treatment was continued up to 11 months. Skin sensitivity persisted during treatment. In cases complicated by rhinitis no evidence was found that infective foci in the sinuses were cleared by cortisone.

H. Herxheimer

1291. **Clinical Studies with Cortisone by Mouth, Cortisone by Injection, and ACTH in the Treatment of Asthma**
W. FRANKLIN, F. C. LOWELL, I. W. SCHILLER, and H. D. BEALE. *Journal of Allergy* [*J. Allergy*] **23**, 27–31, Jan., 1952. 4 refs.

In a study in Boston, Massachusetts, 25 patients with severe asthma received 80 mg. of ACTH or 100 to 300 mg. of cortisone daily. The smallest effective dose was 100 mg. of cortisone and 40 mg. of ACTH. In 17 patients temporary relief was complete, in 6 others partial. Two patients who failed to improve with 120 mg. of ACTH had complete relief after 200 mg. of cortisone. Oral cortisone acted more quickly than cortisone by injection. *H. Herxheimer*

1292. **Behavior of Allergic Skin Reactions after ACTH Therapy.** [In English]
H. HAXTHAUSEN. *Acta Allergologica* [*Acta allerg., Kbh.*] 4, 305–307, 1951.

ACTH has been reported to be of value in allergic skin complaints. In a study at the Rigshospital, Copenhagen, it was found that the immediate urticarial skin response was in no way changed after 5 days' ACTH therapy. Eczematous allergic responses produced electrophoretically in sensitive patients, and tuberculin-type responses obtained by intracutaneous injection, were likewise uninfluenced by ACTH treatment. Also, in guinea-pigs which had been sensitized by dinitrochlorbenzene, ACTH had no effect on the sensitizing process.

A. W. Frankland

1293. **Studies on the Urinary Excretion of 11-Oxycorticosteroids by Allergic Patients Treated with Adrenocorticotropic Hormone (ACTH)**
A. J. STANLEY, G. S. BOZALIS, D. H. HUFF, V. D. CUSHING, and L. CAWLEY. *Annals of Allergy* [*Ann. Allergy*] **9**, 741–752, Nov.–Dec., 1951. 7 figs., 12 refs.

ACTH, 80 mg. daily, was given to 20 patients suffering from allergic asthma and in status asthmaticus. When a satisfactory response was obtained this amount was gradually diminished. In 18 cases the symptoms ceased completely within 6 days. The subjective improvement started within 24 to 48 hours, and marked objective improvement was noted within 48 to 96 hours. The sputum became more liquid and much reduced in quantity and the cough ceased. The vital capacity increased in 7 cases from 50% to 86% of the expected value. The excretion of 11-oxycorticosteroids, which was determined in 11 cases by the method of Corcoran and Page, did not parallel either the dose of ACTH or the clinical response. In some patients there was a marked increase during the treatment, whereas in others there was only a slight day-to-day variation.

H. Herxheimer

1294. **Oral Cortisone Therapy in Ragweed Hay Fever**
E. SCHWARTZ, L. LEVIN, H. LEIBOWITZ, J. REICHER, J. F. KELLY, M. WALLMAN, and T. MCG. FEINBLATT. *Journal of Allergy* [*J. Allergy*] **23**, 32–38, Jan., 1952. 12 refs.

At the Long Island College Hospital, New York, 25 patients suffering from ragweed hay-fever, and in some cases also from asthma, received 100 mg. of cortisone in 4 daily doses during 15 days. During this period they continued with a course of hyposensitization, but had no other anti-allergic treatment. Although previous hyposensitization had not brought relief, cortisone produced excellent or marked relief in 21, moderate relief in 1, and no relief in 3 cases. One case not relieved with 100 mg. of cortisone was completely relieved by 200 mg. The maximum relief was obtained usually on the third day of treatment, and in 15 patients the symptoms returned within 48 hours after discontinuation.

H. Herxheimer

1295. **Urticaria due to Pollen**
G. L. WALDBOTT and K. MERKLE. *Annals of Allergy* [*Ann. Allergy*] **10**, 30–35, Jan.–Feb., 1952. 8 refs.

The authors present 12 cases in which urticaria was confined to the pollen season. In 7 of these there was skin sensitivity to ragweed, in 5 to grasses (including one also sensitive to ragweed), and in one to oak and walnut. In 2 of them urticaria could be provoked by blowing pollen into the patient's nose. Treatment with pollen extract was successful in 7 cases. *H. Herxheimer*

Metabolic and Nutritional Disorders

1296. **Osteomalacia and Renal Glycosuria in Adults. Metabolic Investigation of a Case with Particular Reference to its Relation to the Fanconi Syndrome and to Treatment**

I. A. ANDERSON, A. MILLER, and A. P. KENNY. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **21**, 33–60, Jan., 1952. 4 figs., bibliography.

The case is reported of an adult female patient with severe osteomalacia, hypophosphataemia, mild acidosis, and renal glycosuria. Metabolic studies showed that certain other manifestations of the Fanconi syndrome were present.

The metabolism of calcium and phosphorus was studied during treatment successively with vitamin D, Shohl's citric-acid–sodium-citrate solution, a high intake of calcium and phosphorus, and methyl testosterone, with the following results. (1) Vitamin D in a moderate dose increased the retention of calcium and phosphorus, but in high dosage had a deleterious effect on the calcium balance. (2) Shohl's solution produced a well-marked increase in the retention of calcium and phosphorus, and caused the serum-phosphorus to rise to a normal level; at the same time it brought about rapid relief of the bone pain and tenderness. (3) A high intake of calcium and phosphorus enhanced the effect of Shohl's solution on the retention of these substances. (4) Increase of the dose of Shohl's solution to the high level of 200 ml. per day caused a fall in the serum alkaline phosphatase activity to an essentially normal level, and led to a considerable recalcification of the skeleton and healing of the numerous pathological fractures. (5) Methyl testosterone in a dose of 25 mg. orally per day increased the retention of calcium, phosphorus, and nitrogen, and caused a fall in the excessive ammonia and amino-nitrogen excretion in the urine. The action of the androgen on mineral metabolism is considered to be due either to the relief of a superadded disuse osteoporosis or, in view of its effect on ammonia and amino-nitrogen excretion, to a beneficial action on the disordered renal tubular function.

There was no apparent disorder of citric acid excretion. The administration of methyl testosterone led to a diminution in the urinary excretion of citric acid.

Attention is drawn to a group of similar adult cases in the literature, which presents three common features —bone lesions, hypophosphataemia, and renal glycosuria. Correlation of their clinical and biochemical manifestations suggests that these cases presented other features of the Fanconi syndrome.

The hypothesis is advanced that this group of cases represents a mild or variant form of the Fanconi syndrome in which major symptoms do not arise until adult life, but which may manifest itself in a mild form in early childhood, simulating nutritional rickets. Patients with the syndrome under discussion should respond to treatment directed towards correction of the metabolic disorder, namely, a high calcium and phosphorus intake, alkalinizing therapy to overcome the acidosis, and vitamin D in moderate doses. The apparent beneficial action of methyl testosterone on certain features of the abnormal metabolism in our patient warrants further investigation of its potentialities in this syndrome.—[Authors' summary.]

1297. **A Metabolic Study of the Disturbances Taking Place during Diabetic Coma and its Treatment, with Special Reference to the Changes in Potassium Metabolism.** [In English]

A. F. WILLEBRANDS, J. GROEN, and M. FRENKEL. *Acta Medica Scandinavica* [*Acta med. scand.*] **141**, 331–351, Feb. 4, 1952. 5 figs., 37 refs.

An earlier study (Frenkel *et al.*, *Arch. intern. Med.*, 1947, **80**, 728) of a patient in diabetic coma in whom muscular weakness and respiratory and cardiovascular disturbances occurred during treatment and were associated with a low serum potassium level led the authors to examine further the question of potassium metabolism in diabetic coma in 3 men and 2 women, aged 29 to 63 years, 3 of whom had had diabetes for 18 years, one for 4 years, and one for 1 year. In one case pneumonia was the factor which precipitated coma, but failure to adhere to diet was the cause in the remainder. The blood sugar levels ranged from 175 to 920 mg. per 100 ml. on admission. After initial intensive treatment with insulin and intravenous saline, followed by oral fluids, a diet consisting of rice, butter, and sugar, chosen because of its low potassium and nitrogen content, was given for periods of 1 to 12 days. [For the exact composition of this diet reference should be made to the original.] Potassium was added to the mixture during the latter part of the period in 2 cases, and casein and desiccated beef serum were added for the last 2 days in a third case to increase the nitrogen intake without significantly increasing that of potassium.

During coma, the serum sodium and chloride levels were almost normal in all cases, and in 3 cases in which the alkali reserve was low and dehydration severe the serum potassium level was high. In all cases the serum potassium level fell below the normal during treatment of coma, though there was no clinical evidence of potassium depletion, reaching the lowest level (2·5 to 3·0 mEq. per litre) after 1 to 3 days. This hypopotassaemia persisted for several days, even when the diet was supplemented with potassium. At the same time the urinary potassium content, high during coma, fell during treatment and remained well below normal for some days, there being potassium retention in all cases. The negative nitrogen balance of coma was quickly restored by treatment, and equilibrium was reached by the second day. The authors suggest that the fall in the serum potassium level was not due entirely to dilution of the extracellular fluid by the saline administered intravenously, because the decrease was too great and because

potassium given orally was retained for some days without a rise in serum level. On the other hand, the intracellular fluid lost, together with potassium, during coma has to be made up, and potassium is required in the process of glucose deposition in the liver and muscles under the action of insulin. In the absence of nitrogen retention it can be assumed that none of the potassium retained was due to replacement of tissues destroyed during coma. It was noted that sodium bicarbonate infusions did not affect potassium metabolism. As with potassium, phosphate excretion was high in coma, decreased rapidly, and returned to normal with the introduction of phosphate in the diet, equilibrium being reached in 2 days. The deficit of phosphate was estimated at about 1·0 g. and that of potassium was 10 to 12 g., and was made up in 4 to 6 days. A high blood urea level with low blood pressure was found in 2 cases, and led the authors to suggest that severe coma may cause adrenal cortical hypofunction and so lead to changes in potassium metabolism. The absence of clinical signs of potassium depletion was due to the fact that the serum level in all cases was above 2·5 mEq. per litre. The authors did not think that administration of potassium in large doses is advisable in diabetic coma in view of the possible induction of cardiac irregularities, but they consider that foods containing potassium ought to be given as early as possible. *R. St. J. Buxton*

1298. **Effects of Glucose Administration on the Potassium and Inorganic Phosphate Content of the Blood Serum and the Electrocardiogram in Normal Individuals and in Non-diabetic Patients.** [In English]
J. GROEN, A. F. WILLEBRANDS, C. E. KAMMINGA, H. K. VAN SCHOTHORST, and E. G. GODFRIED. *Acta Medica Scandinavica* [*Acta med. scand.*] **141**, 352–366, Feb. 4, 1952. 8 figs., 24 refs.

The authors noted that large doses of insulin caused a fall in the serum potassium level in patients with diabetic coma, and other experimental work led them to conclude that injection of insulin might have this effect in normal subjects. They therefore investigated the effect of insulin on 6 non-diabetic patients (2 with functional nervous disorders and 4 with prolapsed intervertebral disks), who were given a low-potassium diet of rice, butter, sugar, water, and tea for 2 days. An intravenous infusion of glucose (100 to 150 g.) was started in the morning of the third day in order to stimulate the secretion of insulin, and its effects on the serum potassium level were observed in blood samples taken at 5 p.m. and 10 p.m., and another the following morning. Electrocardiograms were taken at the same time. The test was repeated 2 days later, the patient continuing on the diet. Further observations were made on another group of 6 patients in which the regime was modified, a low-potassium diet being given for varying periods before the glucose infusion, and several receiving only intravenous fluids throughout the test.

On studying the electrocardiograms, only one from the first group was thought to be abnormal, but 4 from the second, the changes being depression of the T wave in one or more standard limb leads and a prolonged Q–T interval. These changes were found only when the serum potassium level was below 3·6 mEq. per litre, and reverted to normal when the level rose above this point. The serum potassium level in most cases decreased with the infusion and continued to fall subsequently, but the patients varied in the degree of their response, the level remaining unchanged in one patient with polyneuritis. The serum inorganic phosphate level fell earlier, and returned to normal more quickly, than that of potassium. The authors concluded that transfer of potassium and phosphate to the intracellular space occurs whenever there is glucose storage in muscle, this explaining why there was no decrease in serum potassium level in the polyneuritic patient with atrophic muscles. The reason for the potassium migration, in their opinion, is to neutralize the acid liberated in the phosphorylation of glucose by adenosine triphosphate. The inorganic phosphate is probably used to rebuild the latter compound, but accompanies the potassium first to maintain intracellular electrical equilibrium.

The authors do not give their results in very great detail, and state that their conclusions are only tentative.
R. St. J. Buxton

1299. **Irreversible Post-hypoglycemic Coma**
J. F. FAZEKAS, R. W. ALMAN, and A. E. PARRISH. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **222**, 640–643, Dec., 1951. 29 refs.

The authors studied the cerebral blood flow and the cerebral oxygen consumption in 4 patients who had suffered from severe hypoglycaemic coma and who did not recover consciousness in spite of correction of the low blood sugar level. Two of the patients were admitted to hospital in deep coma due to hypoglycaemia of unknown duration and degree. In the other 2 patients hypoglycaemia had been inadvertently induced during a vigorous course of treatment for diabetic acidosis [illustrating the danger of giving large doses of insulin]. One patient survived for 72 hours after the hypoglycaemia had been corrected, another for 1 week, the third for 2 weeks, and the fourth for 3 weeks.

The most striking finding was a diminution in the cerebral oxygen consumption in all of these patients, the diminution being most marked in the patient who survived for the shortest time. Repeated determinations of the cerebral blood flow in the patients who survived 3 and 2 weeks respectively showed that, whereas at first it was normal, as time went on it decreased. At no time, however, was it so low that the cerebral tissues would have suffered from anoxia or lack of essential circulating nutrients. An electroencephalogram in 3 patients showed generalized slow delta-wave activity (3 to 5 per second) of moderate voltage. The tracings were similar to those obtained by other workers in acute hypoglycaemia, although in the authors' patients the blood sugar level had been restored to normal when the tracings were taken.

The authors conclude that the profound hypoglycaemia had resulted in such destruction of cellular enzymes in the cerebral tissue that normal metabolism could not be restored. *G. A. Smart*

Digestive Disorders

1300. **Unfavorable Course of Gastric Ulcer during Administration of ACTH and Cortisone**
J. B. KIRSNER, A. P. KLOTZ, and W. L. PALMER. *Gastroenterology* [*Gastroenterology*] **20**, 27–29, Jan., 1952. 11 refs.

Ulcer symptoms recurred soon after the administration of ACTH in 2 patients with gastric ulcer; in one a previously demonstrated crater increased in size; in the other case the ulcer recurred and perforated after 21 days of ACTH. In the third patient a huge gastric ulcer developed within 10 days after the administration of cortisone. An increased output of acid gastric juice was demonstrated in the 2 patients in whom such studies were made.—[Authors' summary.]

1301. **Chronic Stress and Peptic Ulcer—I. Effect of Corticotropin (ACTH) and Cortisone on Gastric Secretion**
S. J. GRAY, J. A. BENSON, R. W. REIFENSTEIN, and H. M. SPIRO. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1529–1537, Dec. 15, 1951. 4 figs., 28 refs.

The authors present evidence that prolonged administration of ACTH produces an increase in gastric acidity and gastric pepsin with subsequent peptic ulceration, perforation, or haemorrhage.

ACTH was given intramuscularly in doses of 100 to 160 mg. daily for 3 to 4 weeks to 6 patients with a normal stomach, one patient with a gastric ulcer, and one with a healed duodenal ulcer. Observations were made on gastric juice collected by continuous aspiration over a 12-hour period at night, and on gastric juice obtained the following morning in 3 to 5 consecutive 15-minute aspirations with constant suction. At the same time 24-hour uropepsin excretion was determined. These studies revealed that ACTH produced a marked increase in the nocturnal and fasting secretion of acid and pepsin to a level equal to that found in cases of active duodenal ulcer. The maximum effects were observed after 7 to 14 days of continuous administration of the hormone. Uropepsin excretion was also raised to a level similar to that observed in patients with active duodenal ulceration.

Accounts are given of exacerbation of the symptoms of gastric ulcer in one case, of fatal gastric haemorrhage in 2 others, and of fatal duodenal perforation in a fourth, all of which occurred while ACTH was being administered. Cases are described to illustrate the effect of anoxia in producing gastric haemorrhage or perforation. In one patient with a brain tumour involving the hypothalamus gastric haemorrhage occurred, and in this case extremely high values for gastric pepsin and urinary uropepsin excretion were observed.

The authors state that the importance of stress factors in the pathogenesis of peptic ulcer has been established. They suggest that chronic emotional and physical stress affect the stomach by a hormonal mechanism acting through the hypothalamus, pituitary, and adrenal cortex; cortisone or similar substances are then liberated as a result of adrenocortical stimulation, and these act on the stomach. *C. E. Quin*

1302. **The Treatment of Peptic Ulcer with an Extract of Pregnant Mare's Urine ("Uroenterone"). Preliminary Report.** (Tratamento das úlceras gastroduodenais pelo extracto de urina de éguas prenhes, denominado uroenterona. Comunicação prévia)
M. F. GARCIA and V. CÔRTES. *Revista Brasileira de Gastroenterologia* [*Rev. brasil. Gastroent.*] **3**, 651–654, Nov.–Dec., 1951. 5 refs.

In the opinion of the authors "uroenterone" is superior to "antelone" and "urogastrone" in the treatment of peptic ulcer. It acts by reducing gastric secretion and preventing a recurrence of ulceration. A total of 36 cases were treated. The period of ulceration was from 28 days to 17 years, the age limits were 16 to 72 years, and males predominated. The patients were divided into 2 groups, the first (28 cases) receiving uroenterone only, the second (8 cases) uroenterone and belladonna. Each patient received 300 mg. of uroenterone daily, in divided doses. Of the patients in the first group, 9 were relieved at once and 9 in 4 to 5 weeks; 10 were unrelieved. In the second group, 5 were immediately benefited, one by the end of the third week, and 2 were unchanged. Thus of the 31 patients who completed the treatment (5 could not be traced) 22 were cured, as judged from clinical and radiological observation.
Paul B. Woolley

1303. **Physiology of Gastric Secretion and its Relation to the Ulcer Problem**
L. R. DRAGSTEDT, H. A. OBERHELMAN, and E. R. WOODWARD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1615–1620, Dec. 22, 1951. 13 refs.

[In abstracting this survey of the mechanisms of gastric secretion reference can be made only to the more important points.]

Gastric juice of a constant acidity is secreted both in healthy subjects and in patients with duodenal ulcer, the abnormality in the latter consisting in the larger volume secreted. Quantitative methods of collection are therefore necessary for the proper assessment of this abnormality. Continuous aspiration of the fasting stomach for 12 hours and estimation of the total quantity of hydrochloric acid recovered is regarded by the authors as the most useful procedure, although the loss of varying amounts of juice through the pylorus introduces an error. The average volume of the 12-hour night secretion in 135 patients with duodenal ulcer was nearly four times that of 81 normal subjects. It is suggested that when very large amounts of hydrochloric acid are secreted during

the night any tolerable regimen of medical management will fail to secure healing of an ulcer.

In patients with duodenal ulcer the gastric secretory response to insulin and histamine is exaggerated: response to the former is abolished and to the latter diminished by complete vagotomy. Of the authors' 470 cases of duodenal ulcer subjected to vagotomy by the abdominal route a positive gastric response to insulin was obtained 10 days after operation in 10%, and in many more after longer intervals. However, in 15 patients observed for 5 years the average percentage reduction in output of hydrochloric acid in the 12-hour night sample remained unaltered despite the fact that the response to insulin was positive in 8 cases. Together with evidence from animal experiments this suggests that a meagre persistence of vagal innervation may not be of any very great clinical importance.

In 307 patients whose pre- and post-operative nocturnal acid secretion was determined there was a general correlation between the percentage reduction obtained and the incidence of negative responses to insulin. Moreover, out of a group of 111 patients with duodenal ulcer treated by vagotomy, the ulcer recurred in only 6 of the 85 in whom there was a post-operative reduction in nocturnal acid secretion of 80% or more, whereas of the 5 in whom the reduction was 20% or less, all suffered recurrence. Other evidence, clinical and experimental, is also adduced to demonstrate the causal relationship between hypersecretion (usually nervous, but in some cases possibly hormonal, in origin) and peptic ulceration. However, in patients with gastric ulcer the acid secretion is often within normal limits and here a failure of the protective mechanism must be postulated.

The authors claim that hypersecretion of acid may be reduced to normal or subnormal levels in 97% of patients by transabdominal, supradiaphragmatic section of the vagi; failure of an ulcer to heal, or its recurrence, is usually due to incomplete denervation, as shown by a positive insulin response and nocturnal hypersecretion 6 months or more after operation. Persistence of vagal function is the chief weakness of this method of treatment. [Such persistence of nervous function is in keeping with experience in the surgery of other parts of the autonomic nervous system.] *C. J. Longland*

1304. **Correlation of Secretory Patterns of Gastric Mucous Substances with Gastroscopic Findings in Humans; their Significance for the Diagnosis of "Atrophic Gastritis"**

G. B. J. Glass, H. Barowsky, and S. A. Schwartz. *Gastroenterology* [*Gastroenterology*] **19**, 829–842, Dec., 1951. 1 fig., 43 refs.

The relationship of the gastroscopic appearance of the gastric mucosa and the secretory pattern of the stomach is the subject of the present article from the New York Medical College. The authors studied 50 patients; these included 10 cases of "atrophic gastritis", 10 cases of "hypertrophic gastritis", 10 cases of superficial gastritis, 10 cases of peptic ulcer with normal mucosa on gastroscopy, and 10 controls. The fasting gastric content was aspirated before gastroscopy and used for determinations of acidity and mucoprotein and mucoproteose concentrations. The last two substances were determined by a colorimetric method (Glass and Boyd). The insulin test was also employed to elicit a maximum secretory response.

There was found to be no relationship between the secretory responses and the gastroscopic diagnosis of hypertrophic or superficial gastritis. In atrophic gastritis the gastric acid was reduced or absent, and the mucoproteose concentration was high. The achlorhydria is attributed to the impairment of functional activity of the mucosal glands in atrophic gastritis, and the high mucoproteose content to a breakdown of mucus from columnar cells of the gastric mucosa. The causes of atrophic gastritis are discussed, and the possibility that glandular mucoprotein may be the substance responsible for intrinsic-factor activity in human gastric juice is thought worthy of further study.

I. McLean-Baird

1305. **Functional Disorders of the Pylorus, with Particular Reference to Achalasia and Acleisia.** (Condizioni funzionali del piloro con particolare riguardo alla acalasia ed alla acleisia)

A. Rollandi. *Radiologia Medica* [*Radiol. med., Torino*) **37**, 817–841, Oct., 1951. 2 figs., bibliography.

In the first part of this paper the author gives a detailed account of the anatomy and physiology of the pylorus, taking into consideration the international literature. He describes not only the pyloric sphincter, but also associates himself with those authors who believe in the existence of a special dilator muscle in this region. Gastric emptying, he believes, is fundamentally regulated by the pylorus, although he admits that other factors, chiefly gastric tone, may play a part. [Unfortunately, no mention is made of the work of Quigley (*Amer. J. dig. Dis.*, 1943, **10**, 418), who showed that gastric evacuation is mainly regulated by the pressure gradient from stomach to duodenum and that the action of the pylorus plays a minor part only. The experiments of Crider and Thomas (*Amer. J. dig. Dis.*, 1937, **4**, 295), who showed that gastric evacuation remains essentially unchanged when the pylorus is kept open by a metal spool, are also not discussed.]

In the second part of the paper two pathological conditions of the pylorus are discussed. The first is a non-spastic closure of the pylorus, which is associated with many gastric and extragastric abnormalities. This condition the author believes to be analogous to Hurst's achalasia of the cardia.

The second is the reverse condition—a prolonged patency of the pylorus for which the author has coined the expression "acleisia" (meaning non-closure), and which he attributes generally to a defective contraction of the sphincter, and only occasionally in hypertonic stomachs to abnormal contraction of the "dilator muscle". This patency of the pylorus, which again is associated with manifold pathological changes, may be looked upon as a valuable indication of some departure from the normal in the gastrointestinal tract, or possibly even in other parts of the body. *R. Schneider*

1306. **Differentiation of Benign and Malignant Diseases of the Gastric Antrum**
C. A. Flood and G. C. Hennig. *Gastroenterology* [*Gastroenterology*] **19**, 787–796, Dec., 1951. 3 figs., 8 refs.

A study of 103 patients with pyloric antral deformities was made by the authors at the Presbyterian Hospital, New York; all the patients had barium-meal and gastroscopic examinations. The series can be divided into two groups: (1) 73 patients with benign antral disease; (2) 30 patients with carcinoma of the pyloric antrum.

The diagnosis of " benign " antral disease was verified by pathological examination in 27 cases, and in the remaining 46 patients by a benign clinical course for at least 6 months subsequently. The clinical picture of benign antral disease was found to resemble peptic ulcer, and evidence of peptic ulcer was found in 60 patients in this group. The radiological abnormalities were narrowing, spasticity, or irregularity in the contour of the antrum, and in 40 cases the suspicion of malignancy was raised. Gastroscopy revealed benign findings, either gastritis or ulcer, in all but one patient. In this case an irregularly nodular mucosa in the distal antrum was thought to be malignant, but at operation was found to be due to hypertrophic gastritis. Some doubt as to the possibility of early malignancy was expressed on gastroscopy in 3 other patients.

In the 30 cases of carcinoma of the pyloric antrum, radiological findings were suggestive of neoplasm in most cases, but the possibility of benign disease was considered in 16 cases; the gastroscopy findings were considered suggestive of malignancy in 20 cases, and closure of the pylorus was observed in only 6 individuals in the entire group of patients with neoplasm. There were 10 patients in whom gastroscopy did not reveal the presence of a neoplasm, and the pylorus was seen in only 3 patients in this group. These patients proved to have small carcinomata, and 2 of the tumours were situated at the pylorus.

The authors consider that gastroscopy cannot be relied on absolutely to exclude carcinoma of the pyloric antrum, but if pyloric closure can be visualized and nothing is seen which suggests carcinoma, the presence of malignant disease is unlikely. *I. McLean-Baird*

1307. **A Contribution to the Treatment of Acute Pancreatitis.** (Contribuição ao tratamento das pancreatiets agudas)
O. F. Longo and C. Sosa Gallardo. *Revista Brasileira de Gastroenterologia* [*Rev. brasil. Gastroent.*] **3**, 627–636, Nov.–Dec., 1951.

The authors review the various theories concerning the aetiology of acute pancreatitis and its treatment. Stress is laid on the advantages of medical treatment; surgery should be reserved for biliary factors which predispose to the pancreatitis.

The fundamental points in treatment are to rest the pancreas, relieve pain, eliminate the aetiological factor, and restore the electrolyte balance. Such measures as the giving of atropine to paralyse the vagus, gastric aspiration, and other procedures are critically analysed. The authors consider that morphine is contraindicated as a pain-relieving agent, and that intravenous procaine, which paralyses the sensory nerve endings of the splanchnic nerves, is superior to splanchnic block. They also recommend giving calcium when correcting the electrolyte balance. Intravenous procaine appears to neutralize overactivity of both the sympathetic and parasympathetic nervous systems, and it certainly relieves the agonizing pain of acute pancreatitis. It reduces spasm in the sphincter of Oddi, and by its anaesthetic properties prevents the deleterious effects on the blood vessels of nociceptive impulses from the affected area. Thus it acts as a general stimulant and tends to maintain the blood pressure in cases of severe shock. It would appear that the procaine tends to concentrate in the affected area.

The authors advise a trial dose of procaine before embarking on the treatment. They use two methods—either 10 to 20 ml. of 1% solution injected intravenously and repeated every 3 or 4 hours, or by slow drip infusion giving 1 to 3 g. daily (1 g. in 500 ml. of fluid). In both methods the initial injection was 20 ml. of 1% solution, together with 500 mg. of ascorbic acid. A total of 26 cases have been treated, many of them serious, with a mortality of 8%; the authors consider these results to be highly satisfactory. Headache may occur but is not dangerous.

[The authors do not mention the number of cases which were subject to toxic effects, and the paper would be of greater value had more space been allotted to analysing the results in greater detail.]

Paul B. Woolley

1308. **The Differential Diagnosis of Jaundice by Means of Liver Function Tests**
G. P. Baker. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **100**, 342–351, 1951. 26 refs.

In this paper 54 cases previously reported (*Guy's Hosp. Rep.*, 1951, **100**, 238) are analysed to assess the value of liver function tests as a guide in the differential diagnosis of jaundice. The tests employed were the qualitative van den Bergh reaction; estimation of serum protein concentration, hippuric acid excretion, urinary urobilinogen content, and serum cholesterol and alkaline-phosphatase levels; and one or other of the flocculation tests [which ones were used is not clear]. The findings confirm those of other workers that the combination of a raised phosphatase level (above 30 King–Armstrong units) with normal (that is, negative) flocculation reaction almost always indicates an obstructive jaundice, whereas a phosphatase level below 30 units combined with a positive flocculation reaction almost always points to hepatitis.

Of the 54 cases, liver tests afforded a correct diagnosis in 39, an indefinite diagnosis in 12, and a wrong diagnosis in 3. The author [rightly] stresses the need for assessing the significance of such tests in correlation with the clinical diagnosis, and no new conclusions are recorded.

Thomas Hunt

See also Pathology, Abstract 1203.

Cardiovascular Disorders

HEART

1309. **Genesis of the Electrocardiographic Pattern of Digitalis**

H. LEVINE, L. H. NAHUM, H. M. GELLER, and R. S. SIKAND. *American Journal of Physiology* [*Amer. J. Physiol.*] **167**, 726–731, Dec. 1, 1951. 2 figs., 17 refs.

Evidence is adduced from experiments at the Yale University School of Medicine, New Haven, Connecticut, to support the hypothesis that the basic mechanism for the development of the electrocardiographic pattern of digitalis is slowing of repolarization in the apical region. The observations were made in normal dogs following the intravenous administration of " cedilanid " (lanatosid C). The characteristic electrocardiographic changes produced in this way were: depression of the ST segments and flattening of T in the precordial leads, followed by increased depression of ST and deep inversion of T. In VF the changes were depression of ST and inversion of T; and in VR there were elevation of ST and an upright T. Evidence is presented to show why these changes must have occurred through either slowing of repolarization in the apical region or acceleration in the basal region. It is a pattern which closely resembles that obtained experimentally when apical repolarization is slowed by local cooling. It is shown that no shortening of Q–T occurred following the injection of cedilanid, and at times there was actual lengthening. As it is known that the Q–T interval roughly represents the repolarization rate of the slowest fibres (those at the base), lengthening of, or no change in, the interval indicates slowing of repolarization in the apical region. It is also shown that heating altered the digitalis pattern and shortened the Q–T interval; when the temperature returned to normal the digitalis pattern reappeared, with lengthening of the Q–T interval. This again supports the authors' hypothesis, as it has been demonstrated previously that the induction of artificial hyperthermia induces the same electrocardiographic changes as are produced by acceleration of apical repolarization by local heating. Finally, the ectopic beats induced by cedilanid were of a configuration which is known to be that of ectopic beats formed near the left apical region.

William A. R. Thomson

1310. **Electrokymography—Preliminary Studies**

L. G. DAVIES and G. R. VENNING. *British Heart Journal* [*Brit. Heart J.*] **14**, 33–41, Jan., 1952. 13 figs., 17 refs.

At the Cardiff Royal Infirmary 50 normal subjects and 25 subjects with abnormal hearts were studied with the Sanborn electrokymograph in conjunction with the direct-writing 4-channel " poly-viso " recorder. The electrocardiogram and phonocardiogram (of limited sensitivity) were recorded synchronously with the electrokymogram.

Aortic and pulmonary artery movements produced records similar in form to mechanically recorded arterial pulse tracings, showing a dicrotic notch. The interval between the beginning of the QRS complex and the onset of aortic or pulmonary artery pulsation was $0{\cdot}12 \pm 0{\cdot}04$ second. This was 0·035 second longer than the corresponding interval reported from pulmonary artery pressure tracings obtained by cardiac catheterization.

Left ventricular movements had different patterns when recorded from different levels, and with the subject in the antero-posterior, 2nd oblique, or intermediate positions. Inward movement of the left ventricle has been described as corresponding with systole, but the authors found that in certain views this could not have been so, for it occurred after the second heart sound. They conclude that a single tracing may thus be misleading, and in view of the complexities of ventricular movement they are so far prepared to draw only limited conclusions from records of abnormal hearts. A method of recording electrokymograms from 9 positions on the left ventricular border is described and recommended. *J. A. Cosh*

1311. **Ligation of the Vena Cava in the Treatment of Heart Failure**

P. COSSIO. *American Heart Journal* [*Amer. Heart J.*] **43**, 97–102, Jan., 1952. 1 fig., 12 refs.

Over a period of two years the author observed in detail 90 cases in which ligation of the inferior vena cava was carried out for uncontrollable heart failure. The surgical mortality was initially 25%; it was soon reduced to 6%. Early improvement, sometimes most surprising, was observed in 70% of the patients and was maintained for months or even years in 56%, provided medical treatment was continued. The early improvement is attributed to the reduction of blood return to the heart and the later improvement to the formation of a lake of blood with a slower return in the recumbent position and also to the elimination of the source of microemboli.—[Author's summary.]

1312. **The Response of Patients with Congestive Heart Failure to a Rapid Elevation in Atmospheric Temperature and Humidity**

G. S. BERENSON and G. E. BURCH. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **223**, 45–53, Jan., 1952. 3 figs., 16 refs.

Patients with congestive heart failure were observed under the influence of sudden elevation of environmental atmospheric temperature and relative humidity and their reactions were compared with those of individuals without cardiac disease. The hot and humid surroundings precipitated acute attacks of left ventricular failure

(cardiac asthma), characterized by severe dyspnea, râles, and gallop rhythm, associated with apprehension and panic. The subjects with advanced cardiac disease were less able to combat the stress of environmental heat than were the subjects without cardiac disease. Indications seem to exist for greater use of air conditioning of hospital wards and rooms of cardiac patients. Since the stress of a hot and humid environment is not conducive to physical or mental rest, patients with cardiac disease should benefit considerably by living in a comfortable atmosphere.--[Authors' summary.]

1313. **Chronic Constrictive Pericarditis—I. Some Clinical and Laboratory Observations**
V. A. McKusick. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **90**, 3–26, Jan., 1952. 3 figs., 34 refs.

Clinical details are given of 20 cases of constrictive pericarditis. The pressure curves obtained from the right ventricle were characterized by an early diastolic fall (" dip ") in pressure followed by a rapid rise to a plateau at a high pressure level. This rapid rise in pressure in early diastole is presumably related to the reduced distensibility of the right ventricle as blood flows in from the auricle. A dip also occurred in the auricular pressure curve taken at the same moment, and in one case at operation an identical type of pressure record was obtained from the left ventricle. The pressure dip is closely related to the protodiastolic sound occurring in constrictive pericarditis. Tuberculosis plays a part in aetiology in some cases, but in others trauma may be important. The serum albumin level is occasionally low in constrictive pericarditis, but this may recover very rapidly after operation. Radiologically, dilatation of the superior vena cava with little cardiac enlargement is always suggestive, but localized constriction at the caval orifices was not found. Calcification was present in only half the cases. The condition may closely simulate mitral stenosis.

The results of pericardectomy were, in general, satisfactory. The only deaths that occurred were in patients over 55 years of age. *J. McMichael*

1314. **Chronic Constrictive Pericarditis—II. Electrokymographic Studies and Correlations with Roentgenkymography, Phonocardiography, and Right Ventricular Pressure Curves**
V. A. McKusick. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **90**, 27–41, Jan., 1952. 10 figs., 24 refs.

When electrokymographic tracings are taken in constrictive pericarditis they show that the expansion of the ventricle is more rapid than normal in early diastole, flattening out to a plateau before the next systole. Standstill of the ventricular border for the greater part of diastole means an impediment to ventricular filling in constrictive pericarditis. The abnormal ventricular pressure curves are restored towards a normal pattern by successful operation. The electrokymographic pattern can also be detected in radiokymograms. When electrokymograms are recorded simultaneously with intraventricular pressure curves they show that the early diastolic dip in pressure occurs during the phase of rapid filling of the ventricle. The protodiastolic sound is synchronous with the end of rapid ventricular filling, which presumably is abruptly halted at the beginning of the diastolic plateau; the sound is described as a " water-hammer " phenomenon. *J. McMichael*

1315. **Myocardial Deficiency associated with Lesions of the Brain Stem and its Causation.** (Die Mangeldurchblutung des Herzmukels bei Hirnstammschäden und ihre Ursache)
A. Weber. *Deutsche Medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **76** 1616–1618, Dec. 21, 1951. 2 figs., 8 refs.

Electrocardiograms were recorded in 46 cases of cerebral trauma [apparently mainly concussion] thought to involve the brain stem, with the patient in the recumbent and the erect positions, together with records of the pulse rate and blood pressure. The change from the recumbent to the upright position tended to induce peripheral vasomotor collapse in 35 patients, while in 32 electrocardiographic changes in the S–T levels and T waves suggestive of myocardial ischaemia appeared, only 6 patients remaining unaffected in either respect. With recovery from the trauma these changes disappeared, and their occurrence could also be prevented by firm bandaging of the limbs and abdomen.

[The tracings reproduced are misleading as Leads II and III of the resting electrocardiogram have become interchanged.] *G. Schoenewald*

1316. **The Treatment of Endocarditis Lenta.** (Erfahrungen und Ergebnisse bei der Behandlung der Endocarditis lenta)
K. Spang and U. Meier. *Deutsches Archiv für Klinische Medizin* [*Dtsch. Arch. klin. Med.*] **198**, 728–741, 1951. 1 fig., 19 refs.

This article reports German experiences in the treatment of subacute bacterial endocarditis since the war. The authors' general conclusions are the same as those reached in Great Britain, but they seem to treat a higher proportion of cases in which the blood culture proves negative. For these cases they recommend a combination of penicillin and streptomycin. The ultimate prognosis depends largely on the cardiac state before the endocarditis was acquired. *G. S. Crockett*

1317. **Clinical and Physiological Correlations in Patients with Mitral Stenosis—V**
B. M. Lewis, R. Gorlin, H. E. J. Houssay, F. W. Haynes, and L. Dexter. *American Heart Journal* [*Amer. Heart J.*] **43**, 2–26, Jan., 1952. 7 figs., 26 refs.

The area of the mitral valve and the degree of pulmonary vascular disease have been calculated from physiological data in 30 patients with pure mitral stenosis without evidence of active rheumatic carditis. From a hydraulic point of view, a valve area of 1·0 cm.^{2}, $\frac{1}{4}$ to $\frac{1}{6}$ normal, appears to be a critical one, for at that level of stenosis the pressure head needed to maintain a normal cardiac output approaches the plasma osmotic pressure.

Probably from the stimulus of an increased pulmonary "capillary" pressure, a variable degree of vascular obstruction develops in patients when the mitral valve area becomes reduced to about 1·0 cm.² or smaller. This results in a lower cardiac output, which may protect the capillary bed from sudden increases in pressure.

The clinical picture in mitral stenosis can be explained in a large measure by the interplay of the degree of stenosis with the degree of pulmonary vascular obstruction. The combination of a narrow valve with only a slight increase in pulmonary arteriolar resistance is associated with predominantly respiratory symptoms, exertional dyspnea, hemoptysis, and paroxysmal nocturnal dyspnea, the right ventricle not becoming dilated. The effect of a narrow valve and a high pulmonary arteriolar resistance appears to be additive in causing electrocardiographic evidence of right ventricular hypertrophy and roentgenographic signs of cardiac enlargement. The combination of a narrow valve and great increases in pulmonary arteriolar resistance is associated with severe dyspnea, cardiac enlargement, and signs of right ventricular failure.

Most patients with mitral stenosis can be divided into four general categories by their signs, symptoms, and physiological adjustments.—[Authors' summary.]

1318. **An Anomalous Coronary Artery Arising from the Pulmonary Artery**

E. S. Cronk, J. G. Sinclair, and R. H. Rigdon. *American Heart Journal* [*Amer. Heart J.*] **42**, 906–911, Dec., 1951. 6 figs., 12 refs.

A third case is reported in which the right coronary artery arose from the pulmonary artery, only two such cases having previously been reported in the literature. This patient died at 90 years of age and the condition was found at necropsy; the other two had reached adult life, dying at 30 and 61 years of age respectively. The embryology of this and other similar anomalous coronary-artery malformations is fully discussed.

T. Semple

1319. **Left Coronary Artery from the Pulmonary Artery. Three Cases, One with Cardiac Tamponade**

H. I. McKinley, J. Andrews, and C. A. Neill. *Pediatrics* [*Pediatrics*] **8**, 828–840, Dec., 1951. 14 figs., 13 refs.

The authors report from the Hospital for Sick Children, Toronto, 3 new cases in which the left coronary artery arose from the pulmonary artery, bringing the total of reported cases to 35. In one of the present cases there was myocardial rupture, which has not previously been recorded in this condition. The diagnosis was made before death in all 3 cases with the aid of *x* rays and the electrocardiogram, which showed a low-voltage tracing, inverted T waves in Leads I and III, and a variable degree of left axis deviation. (The diagnosis was similarly made before death in 5 of the 11 cases reported since 1947.) The symptom pattern is one of feeding difficulty at the second or third month of life for which no obvious cause can be found, then intermittent dyspnoea with exertion, and in some cases cardiac angina, which is well and fully described. The desirability of recognition of this pattern is emphasized, as early diagnosis before irreversible myocardial damage has occurred might enable new methods of treatment to be applied, such as the use of vasodilator drugs or surgical measures to increase the left coronary flow by raising the pulmonary pressure, as by the Potts–Smith operation.

David Morris

1320. **Sites of Obstruction to Pulmonary Blood Flow in the Tetralogy of Fallot: an Anatomic Study**

E. C. Burke, J. W. Kirklin, and J. E. Edwards. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **26**, 498–504, Dec. 19, 1951. 5 figs., 6 refs.

The morbid anatomy of Fallot's tetralogy was studied in 26 cases, together with necropsy records and reports selected from the literature in another 22 cases.

Of this series of 48 cases the point of maximum stenosis was in the infundibulum in 29, and in 19 of these the narrowest region was at the ostium. Often there was endocardial thickening of the tract, diffuse or localized; the infundibular wall was relatively thick. In 5 cases equally advanced stenosis was found in the pulmonary valve and in the infundibulum. The pulmonary valve was the narrowest point in 11 cases, 5 with stenosis and 6 with atresia; in one of the latter cases the atresia was believed to be acquired. In 3 cases there was atresia of the pulmonary trunk. Further analysis shows that there was maximal or significant obstruction to pulmonary blood flow in the infundibulum in 43 of the cases; significant obstruction at the level of the pulmonary valve was observed in 29 cases.

These findings, state the authors, agree with other published series, and support the view that in most cases surgical success will not depend alone on pulmonary valvulotomy, but chiefly on modification of the infundibulum.

R. S. Stevens

1321. **Use of Quinidine in Treatment of Chronic Auricular Fibrillation. Results Obtained in a Series of One Hundred Fifty-five Patients**

E. H. Yount, M. Rosenblum, and R. L. McMillan. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 63–69, Jan., 1952. 1 fig., 16 refs.

On the assumption that auricular fibrillation by itself may have deleterious effects on cardiac function, the authors have given oral quinidine—to which, they say, there are no contraindications except sensitivity—to 155 patients with chronic fibrillation, due in most cases to atheroma and rheumatic heart disease. In no fewer than 119 patients was sinus rhythm re-established in an average of 6 days with doses of 0·4 g. 4-hourly and a mean plasma concentration of 9 mg. quinidine per litre. No relation was found between age, cardiac failure, or duration of fibrillation and inability to revert; and since reversion invariably took place at a blood level of 8 to 12 mg. per litre it was not considered justifiable to increase dosage indefinitely in patients who did not respond. A therapeutic blood level was attained in a few hours, with cumulation over the first 3 days; when the drug was discontinued the blood level fell

rapidly, and it seems probable that quinidine is destroyed in the body. The authors consider that about half the therapeutic dose is required for maintenance and may be given 6-hourly.

Toxic symptoms—chiefly gastro-intestinal and vestibular—occurred at a therapeutic blood level and may have been due to the rapidity of rise. It is suggested that the development of flutter is no reason for stopping quinidine, and the previous occurrence of emboli is regarded as an urgent indication for the drug; no embolic episodes occurred during treatment. Only 41 patients have so far been traced, and 6 of these have relapsed in an average period of 6 months after reversion.

A. Paton

1322. **Audible Auricular Heart Sounds in Auricular Flutter**

J. P. RATTIGAN, W. W. BYRNES, H. KRAUS, and H. S. SISE. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 130–131, Jan. 24, 1952, 2 figs., 3 refs.

Two cases of auricular flutter in which audible auricular sounds were graphically recorded are added to the 11 cases previously reported. These cases are of interest in that auricular sounds were recorded at the precordium during ventricular systole in complete heart block, a finding not previously reported, and a graded increase in intensity of the auricular sounds in each cardiac cycle was observed and confirmed by phonocardiogram.—[Authors' summary.]

CORONARY DISEASE

1323. **Complete Functional Recovery after Coronary Occlusion and Insufficiency**

A. M. MASTER and H. L. JAFFE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1721–1726, Dec. 29, 1951. 15 refs.

During the past 25 years the authors were called into consultation in 554 cases of acute coronary occlusion. Of this total 79 patients, of whom 35 died, were seen only in the acute attack, and for various reasons a satisfactory follow-up was not possible in another 63; these patients were excluded from the present investigation. An additional 141 patients were investigated in whom a diagnosis of acute coronary insufficiency had been made. The distinction between coronary insufficiency and occlusion was made on electrocardiographic findings, coronary insufficiency being diagnosed when the T-wave changes and the RS–T depression appeared early and returned to normal in several days or weeks, whereas coronary occlusion was diagnosed when the changes are more marked and more prolonged. The patients were followed up for a period averaging 6½ years (and ranging from 3 months to 29 years).

Of the 412 patients with coronary occlusion, 154 (37·5%) made a good recovery, and 115 (28%) made a satisfactory recovery but continued to have occasional effort angina.

Of the 154 patients who made a complete functional recovery, only 6 (4%) survived less than 5 years, and the total mortality in this group (19%) was less than half of that among the 115 patients who continued to have symptoms (47%); 25% survived more than 10 years, and 40% more than 5 years, 83% being employed during that time. Those who were less than 45 years old at the time of the attack did only slightly better than the older patients. The best prognostic guide after coronary occlusion thus appears to be the patient's symptoms rather than the objective findings. Whether an infarct was anterior or posterior did not appear to influence the future course. The prognosis following acute coronary insufficiency was better than that after coronary occlusion. Only 4% of these patients died, and more than half of them made a complete recovery.

The results as a whole indicate that most patients who survive an attack of coronary occlusion or insufficiency may be encouraged to lead fairly normal lives.

H. E. Holling

1324. **Tromexan in the Treatment of Coronary Thrombosis**

J. A. TULLOCH and A. R. GILCHRIST. *American Heart Journal* [*Amer. Heart J.*] **42**, 864–875, Dec., 1951. 7 figs., 18 refs.

The authors, from the Royal Infirmary, Edinburgh, summarize the literature on the results of anticoagulant therapy in coronary thrombosis, and describe their present regime of treatment. "Tromexan" administered during the first 4 weeks in a dose sufficient to maintain the prothrombin time at a figure 2½ times the normal value is an effective substitute for dicoumarol. By its use the mortality rate during the first 6 weeks of treatment was halved, falling from 40·5%, observed in a previous control series, to 18·4% in this series treated with tromexan. This compares favourably with a mortality of 22·8% in a previous group treated with dicoumarol. An impression was gained that patients treated with tromexan both look better and feel better than do conservatively treated patients. Thrombo-embolic complications were uncommon, the incidence falling from 1 in 4 patients in control groups to less than 1 in 20 patients treated with tromexan. Heart failure with sudden death accounted for most fatalities on this regime of treatment.

T. Semple

1325. **Cerebral Manifestations of Acute Myocardial Infarction**

S. L. COLE and J. N. SUGARMAN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **223**, 35–40, Jan., 1952. 11 refs.

Syncope, convulsions, coma, or hemiplegia may be the only presenting symptoms of acute myocardial infarction.

Six cases are presented in which central nervous system symptoms so dominated the clinical picture that the brain was suspected as the seat of the pathologic process, and the cardiac accident initially was overlooked. No evidence of cerebral thrombosis, embolus, or hemorrhage was found at autopsy. Possible mechanisms to account for the cerebral symptoms on the basis of myocardial infarction are discussed.

An attempt is made to differentiate the picture of acute myocardial infarction with predominantly central nervous system symptoms from the combined acute vascular lesions of the brain and heart. The use of the electrocardiogram, electroencephalogram, and improved pathologic techniques to aid in that differentiation are discussed.—[Authors' summary.]

1326. **Treatment of Shock in Recent Myocardial Infarction by Intra-arterial Transfusion**
E. N. SILBER, B. D. LEVIN, G. H. BECKER, and R. C. LEVY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1626–1629, Dec. 22, 1951. 1 fig., 24 refs.

A profound fall in blood pressure after myocardial infarction is associated with a high mortality, and must lead to a further diminution in coronary blood flow and so cause more extensive infarction and diminish the efficiency of the viable muscle.

For this reason 9 patients with recent myocardial infarction, presenting the clinical picture of severe shock, were treated by infusion of 250 to 500 ml. of oxygenated blood (7 cases) or plasma (2 cases) into the radial artery over a period of 20 to 30 minutes. One patient died during the infusion, 4 were little improved, but 4 showed an immediately favourable response, with a rise in blood pressure to normal levels. Two of this group survived and made an adequate recovery, and 2 died after maintaining a satisfactory improvement for a few days.

[This is a preliminary report, and does not give any very convincing evidence that the procedure described is of value.] *J. W. Litchfield*

1327. **Age and Survival in Cases of Acute Myocardial Infarction**
H. I. RUSSEK, B. L. ZOHMAN, A. A. DOERNER, A. S. RUSSEK, and L. G. WHITE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1731–1733, Dec. 29, 1951. 7 refs.

An analysis was made of the case records of 1,047 patients treated for acute myocardial infarction in the U.S. Public Health Service Hospital, Staten Island, and the Maimonides and King's County Hospitals in Brooklyn. The patients were divided into two groups, with 618 patients under 60 years of age (average age 51·1 years) in one group, and 429 over 60 years (average age 67·4 years) in the other. They were also divided into " good risk " and " poor risk " cases on the basis of their first 24 hours in hospital. The " poor risk " cases had: (1) previous myocardial infarction; (2) intractable pain; (3) severe degree or persistence of shock; (4) significant cardiac enlargement; (5) gallop rhythm; (6) congestive heart failure; (7) auricular fibrillation or flutter, ventricular tachycardia, or intraventricular block; or (8) diabetic acidosis or other serious complicating disease.

The mortality rate was 40·1% in the patients over 60, whereas it was only 28·8% in the patients under 60. However, if the cases were divided into " good risk " and " poor risk " groups it was seen that age was not a significant factor in the outcome of the individual case. Thus it appears that although the mortality rate from acute myocardial infarction increases with the age of the patient, this increase in mortality is the result of a higher incidence of serious attacks.

H. E. Holling

VEINS

1328. **Tromexan Therapy. Dosage and Indications**
C. HOUGIE. *Lancet* [*Lancet*] **2**, 1118–1120, Dec. 15, 1951. 5 refs.

A series of 50 patients with thrombo-embolic disease were treated with " tromexan " (bis-3 : 3′-(4-oxycoumarinyl)-ethyl acetate). The drug was given in 3 or 4 doses daily and an attempt was made to keep the prothrombin concentration, as assessed against plasma dilutions in saline, between 10% and 20%. In most cases this required a daily dosage of 300 to 600 mg. of tromexan. In 3 cases thrombo-embolic complications occurred during treatment, when the prothrombin concentration was between 20% and 30%. *A. Brown*

1329. **Thromboembolic Pulmonary Vascular Sclerosis. Report of a Case following Pregnancy and of a Case Associated with Cryoglobulinemia**
E. E. MUIRHEAD, P. O. MONTGOMERY, and C. E. GORDON. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 41–62, Jan., 1952. 8 figs., bibliography.

Ayerza's syndrome is defined as pulmonary vascular sclerosis of sufficient magnitude to cause cardio-pulmonary failure; 2 cases seen at hospitals attached to the University of Texas are fully described. Extensive clinico-pathological investigation and careful necropsy within 2 hours of death were performed on each subject. [In neither case report, however, is pulmonary blood pressure mentioned, preterminal accentuation of the pulmonary second sound in one patient being the only evidence on this point.]

The pulmonary arterial thickenings and occlusions seen in the first case were thought to be, and probably were, due to organization of multiple minute blood-clot emboli possibly derived from parametrial veins, but this was not conclusively demonstrated. The second case report contains a great many abnormal findings. Some of these were: evidence of treated syphilis, probably still active, at least in the nervous system; systemic hypertension; disseminated plasmacytosis reaching 14·5% of the cells in one spinous process; and hyper- and cryo-globulinaemia. This last finding is emphasized because of the " proteinaceous " nature of the thrombi in this case [although the excellent photographs do not suggest any striking difference between them and the occlusive masses of the other subject]. Both cases had some right-sided cardiac hypertrophy and polycythaemia.

Possible mechanisms of the development of pulmonary sclerosis are discussed and the term " thrombo-embolic pulmonary endarteritis " is suggested as a better description of the condition. These 2 cases are interpreted as supporting this aetiological concept.

J. B. Enticknap

1330. **The Use of Heparin–Gelatin–Dextrose in Venous Thrombosis and Pulmonary Embolism**
C. CRANE. *New England Journal of Medicine* [*New Engl. J. Med.*] **245**, 926–929, Dec. 13, 1951. 15 refs.

At the Brigham Hospital, Harvard Medical School, 100 patients with post-operative deep venous thrombosis or pulmonary embolism for which no cause could be found were treated with daily intramuscular injections of heparin–gelatin–dextrose (" depo-heparin ") to which ephedrine and adrenaline had been added. The daily dose was determined by giving a test dose of 25 mg. of sodium heparin intravenously, clotting time being determined after 20, 40, and 60 minutes. If the peak of the curve was below 20 minutes, the daily dosage was 300 mg.; if between 20 and 50 minutes, it was 200 mg.; if over 50 minutes, 100 mg. was given. [The strength and proportion of ephedrine and adrenaline are not stated.] Treatment was continued for an average of 7 days. Clotting time was determined twice daily, and in 80% it fell to between 15 and 40 minutes, which was regarded as satisfactory.

Half the patients had soreness at the site of injection which lasted about 2 days. In 2 an abscess developed, requiring incision and drainage; 2 others had nausea, numbness, tingling, and blurring of vision soon after the injection; 5 patients bled from the operation site while under treatment; 1 had haematuria; 2 had epistaxis. The therapy was judged to have failed in 7 cases, as 4 of the patients had further pulmonary emboli soon after the conclusion of the course, and 3 others had a recurrence of venous thrombosis; none of the patients with pulmonary embolism died. Good results were therefore obtained in 93% of the cases.

C. W. C. Bain

1331. **A Statistical Study of the Incidence of Fatal Pulmonary Embolism in Freiburg Necropsy Records during the Period 1911–50.** (Statistische Untersuchungen über die Haufigkeit der tödlichen Lungenembolien im Freiburger Obduktionsgut der Jahre 1911–50)
H. G. HILLEMANNS. *Archiv für Kreislaufforschung* [*Arch. KreislForsch.*] **17**, 309–326, Dec., 1951. 5 figs., 33 refs.

This statistical study was made because between 1948 and 1950 the number of cases of fatal pulmonary embolism increased almost twofold. During the 40 years 1911–50 the average incidence of pulmonary embolism in 19,353 necropsies was 3·9%. Before each of the two world wars there was an increase, and after each a decrease, in such cases. For detailed study the years 1937–9, 1946–7, and 1949–50 were selected. Age and sex did not influence the periodic fluctuations of the incidence of pulmonary embolism, but throughout the series the rate in males was 5·14% and in females 8·83%. The state of nutrition of the bodies examined had a definite relationship to pulmonary embolism; even in an average year the less well-nourished provided fewer pulmonary emboli. Mortality from embolism increases considerably with increasing body weight, and obese women are particularly in peril. The over-all increase, apart from the periodic fluctuations, in mortality from pulmonary embolism depends on an over-all increase in thrombosis and in the tendency of thrombi to become detached and lodged in the lungs. This tendency is regarded as due to increasingly vigorous treatment of thrombo-embolic vascular disease. *E. Neumark*

DISORDERS OF CIRCULATION

1332. **The Treatment of Arterial Insufficiency of the Lower Extremities with Intra-arterial Histamine Infusion.** (Intraarterial histaminfusion ved arterieinsufficiens i underextremiteterne)
J. CLAUSEN, E. THERNØE, and P. THERNØE. *Nordisk Medicin* [*Nord. Med.*] **47**, 119–122, Jan. 25, 1952. 2 figs., 14 refs.

The authors have treated 15 patients suffering from arterial insufficiency of the legs with intra-arterial drip infusions of histamine in normal saline by Mufsen's method, in which the needle is inserted into the femoral artery just below the inguinal ligament. Before treatment the condition was assessed by clinical examination, oscillometry, radiography, and walking tests.

Of the 15 patients, 12 were treated as out-patients and had no other treatment; the other 3 were treated in hospital as their condition was so severe that walking to and from hospital was impossible. In these last and in 2 other patients with arteriosclerosis in an advanced stage only symptomatic relief was obtained. In 7 cases 6 to 10 infusions abolished pain and enabled the patient to walk any distance practically without pain. In 3 patients with a long-standing history of intermittent claudication walking tolerance improved only so long as the infusions were being administered, but this improvement soon subsided after treatment was stopped.

The side-effects of histamine, such as flushing, headache, and burning sensation, were never sufficiently severe to require the infusions to be stopped. Local complications were extremely rare. Asthma, diseases of the aorta, gastric ulcer, and severe myocardial degeneration are contraindications. The authors consider intra-arterial histamine infusion to be an easy and effective treatment for peripheral arterial disease which at the same time facilitates diagnosis. *E. S. Fountain*

1333. **The Treatment of Hypertension with the Kempner Diet and a Low-sodium Regimen. Clinical Observations on 600 Cases.** (Tratamiento de la enfermedad vascular hipertensiva con la dieta de Kempner y regimenes hiposódicos. Consideraciones clínicas sobre 600 casos)
F. MONTOREANO and J. RABENKO. *Prensa Médica Argentina* [*Prensa méd. argent.*] **38**, 2849–2856, Nov. 2, 1951. 26 refs.

This is an account from Buenos Aires of a study of 600 patients (382 females and 218 males) between the ages of 28 and 79 with essential hypertension, who were treated with Kempner's rice diet. The diet was given for periods varying from 2 weeks to 4 months; some patients took a modified Kempner's diet intermittently up to 2 years. The majority of patients refused the diet after a time. In about 90% improvement of symptoms was

noted, but 60% complained of weakness. As regards the effect on blood pressure, the systolic pressure was reduced to normal in 69 (11·5%); it fell by over 50 mm. Hg in 156 (26%), 30 mm. Hg in 177 (29·5%), and up to 20 mm. Hg in 174 (29%); no change was noted in 57 (8%); and there was a rise in 36 (6%). The diastolic pressure was reduced to normal in 135 (22·5%); it fell by over 20 mm. Hg in 87 (14·5%), 15 mm. Hg in 174 (29%), and up to 10 mm. Hg in 168 (28%); there was no change in 144 (24%), and a rise in 27 (4%). The heart size was determined radiologically in 106 cases, a reduction being observed in 35. The main change in the electrocardiogram consisted in a reduction in S–T depression. After the rice diet was stopped the blood pressure started to rise in about a fortnight, regaining its original level after a period varying between a few days and several months.

It is concluded that this method is effective in reducing the blood pressure without, however, modifying the course of the disease. *A. Schott*

1334. **The Effect of Application of a Direct Current to the Central Nervous System in Hypertension.** (О влиянии постоянного тока нисходящего направления на кровяное давление при гипертонической болезни)
T. K. Zinzin. *Невропатология и Психиатрия* [*Nevropat. Psikhiat.*] **20**, 54–56, 1951.

According to Pavlov's teaching, hypertension is caused by disturbances in the cortex and hypothalamic nuclei due to the lack of balance between the processes of excitation and inhibition. Previous investigations on the effect of direct current on the central nervous system having shown that such a current applied in a descending direction has a soothing effect, and in an ascending direction an exciting effect, 34 patients were chosen for treatment; 3 of these were cases of essential hypertension, 23 of hypertension with organic changes in the nervous system, and 8 had organic nervous changes but no hypertension.

The anode (8×5 cm.) was placed on the back of the neck and the cathode (10×8 cm.) on the lower thorax and upper lumbar region, and a current of 2 to 20 mA applied for 20 minutes. The systolic blood pressure fell by an average of 23 mm. Hg in 25 patients, while in 4 patients it rose by an average of 15 mm. Hg. In 5 patients it remained unchanged. A fall in diastolic pressure by about 12 mm. Hg was observed in 21 patients, in 4 patients it rose, and in 9 it remained unchanged. The reductions were fairly well maintained.

W. Szaynok

1335. **Experimental Treatment of Hypertension by the Intra-arterial Injection of Procaine Solution.** (Опыт лечения гипертонической болезни внутриартериальным введением 0·5% раствора новокаина (Внутриартериальная новокаиновая блокада))
M. A. Chzanov and R. T. Melamid. *Невропатология и Психиатрия* [*Nevropat. Psikhiat.*] **20**, 56–61, 1951.

The authors report the treatment of 150 patients suffering from hypertension by the intra-arterial injection of 0·5% procaine solution, the effect of which is considered to be due to blocking of the interoreceptors of the arterial intima. The patients ranged in age from 20 to over 60 and included cases of essential and arteriosclerotic hypertension. There were 102 males and 48 females, of whom 76 had severe hypertensive symptoms such as headaches, giddiness, and fainting attacks, with organic nervous changes, while 31 were severe cases of cerebral arteriosclerosis with hemiplegia, aphasia, and similar manifestations.

In each case 10 to 15 ml. of 0·5% procaine solution in normal saline was injected slowly into the femoral artery. In 105 patients there was a fall of 20 to 30 mm. Hg in the systolic pressure and of 10 to 30 mm. Hg in the diastolic 10 minutes after the injection which was maintained for at least 24 hours; 37 patients showed a fall in systolic pressure only, 1 in diastolic pressure only, in 3 patients the blood pressure remained unchanged, and in 4 it rose. After 2 to 3 days the subjective hypertensive symptoms had subsided, and paresis and aphasia were less severe. All patients were observed for periods ranging from 2 months to 2 years, during which the blood pressure remained almost stable in 97% of cases of essential hypertension. In cases with changes in the central nervous system it rose again after an interval of 2 weeks to 4 months, but a second injection stabilized the blood pressure for a long period. The treatment had only a transitory effect on nephrosclerotic hypertension. Previous cardiac infarction is a contraindication. In 2 cases there were mild symptoms of shock, subsiding in 24 hours. The method is recommended as being both effective and safe. *W. Szaynok*

1336. **Subtotal Adrenalectomy in the Treatment of Patients with Severe Essential Hypertension**
H. A. Zintel, C. C. Wolferth, W. A. Jeffers, J. H. Hafkenschiel, and F. D. W. Lukens. *Annals of Surgery* [*Ann. Surg.*] **134**, 351–360, Sept., 1951. 4 figs., 14 refs.

This is a preliminary report on 26 patients in whom subtotal adrenalectomy was performed as a treatment for hypertension. The follow-up period is still too short for any definite conclusions to be reached. However, a definite reduction in systolic and diastolic pressure was achieved in most cases, though some form of sympathectomy had preceded or accompanied the adrenalectomy in 11 of the patients. Adrenal deficiency developed in most of the patients, but substitutive therapy was required in only 3, and then only temporarily. *J. Marshall Pullan*

1337. **The Weight of the Left and Right Ventricles in Hypertension.** (Das Verhalten der Muskelmasse des rechten und linken Ventrikels bei Hypertonie)
H. Merkel and G. Nadolny. *Zeitschrift für Kreislaufforschung* [*Z. KreislForsch.*] **40**, 341–355, 1951. 2 figs., 19 refs.

1338. **Chromaffin Tumour with Chronic Hypertension**
G. Lumb. *British Medical Journal* [*Brit. med. J.*] **2**, 936–938, Oct. 20, 1951. 4 figs., 25 refs.

Disorders of the Blood

1339. **The Anaemia of Scurvy**
A. BROWN. *Glasgow Medical Journal* [*Glasg. med. J.*] **32**, 95–100, April, 1951. 6 figs., 17 refs.

The author describes 43 cases of frank scurvy admitted to two Glasgow hospitals during a 5-year period. Most of the patients were males over 50 years of age who had for many years lived on bread and tea to which tinned milk had been added. Several had previously been admitted to hospital with scurvy. In 9 patients there was little or no anaemia; when present this was sometimes macrocytic, sometimes normocytic, and sometimes microcytic. The bone marrow in 10 patients was normoblastic, in some cases being overactive and in others tending to be aplastic. The author describes in detail 3 cases which responded well to ascorbic acid treatment. Another 3 cases responded clinically to ascorbic acid, but the anaemia improved only when the patients were given a full hospital diet supplemented with autolysed yeast.

The author considers that his findings support the view that scurvy is almost invariably a multiple deficiency disease, and that no single factor can be uniformly effective against the anaemia, though undoubtedly ascorbic acid plays a part in erythropoiesis.

Janet Vaughan

1340. **Intestinal Macrocytic Anaemia**
G. M. WATSON and L. J. WITTS. *British Medical Journal* [*Brit. med. J.*] **1**, 13–17, Jan. 5, 1952. 39 refs.

A macrocytic anaemia with megaloblastic bone marrow sometimes occurs clinically in association with intestinal stricture or after anastomosis. The fundamental abnormality causing the anaemia in these cases appears to be the presence of a stagnant or obstructed portion of small intestine, the contents of which are infected with colonic organisms. Free hydrochloric acid is usually present in the gastric juice, and there is sometimes, but not necessarily, steatorrhoea. Subacute combined degeneration of the spinal cord occurs in a large proportion of the cases. The anaemia responds to liver extract, and to surgical correction of the intestinal abnormality.

The authors attempted to reproduce this syndrome in rats by making a blind, self-filling loop in the upper half of the small intestine. A high proportion of the animals surviving operation developed anaemia in periods ranging from 26 days to 6 months after operation. The anaemia was macrocytic, and the bone marrow of normal or increased cellularity with a shift to the left in the maturation of the erythrocyte series. No typical megaloblasts were seen. Other features were an irregular reticulocytosis, nucleated erythrocytes in the peripheral blood, and the absence of leucopenia. Increased haemolysis was demonstrated by increased faecal excretion of urobilinogen. There was no correlation between the development of anaemia and impairment of fat absorption. Therapeutically, the anaemia responded well to folic acid and aureomycin, but only poorly or not at all to refined liver extract and vitamin B_{12}.

The authors consider that from the evidence available the most likely cause of the anaemia is an alteration in the intestinal flora analogous to that which occurs in gastro-colonic fistula in man, the steatorrhoea being due to the same cause. The intestinal bacteria seem in some way to be concerned with the absorption or utilization of haematopoietic substances.

Ellis Dresner

1341. **Treatment of the Megaloblastic Anaemias with Citrovorum Factor**
L. S. P. DAVIDSON and R. H. GIRDWOOD. *Lancet* [*Lancet*] **2**, 1193–1195, Dec. 29, 1951. 9 refs.

The " citrovorum factor " (folinic acid) is now known to be closely related chemically to folic acid, and is said to have the structure 5-formyl-5 : 6 : 7 : 8-tetrahydropteroylglutamic acid. Its clinical effects in the treatment of human megaloblastic anaemia have been reported to be similar to those produced by folic acid. In this paper are recorded the effects of giving synthetic folinic acid intramuscularly or orally in doses ranging from 3 to 12 mg. over varying periods to 6 patients with pernicious anaemia, 2 with megaloblastic anaemia of pregnancy, and 1 with idiopathic steatorrhoea and megaloblastic anaemia. In all of them the haematological response was satisfactory and similar to that produced by folic acid. [From the figures given, repeated doses of 3 mg. daily by mouth, or a single intramuscular dose of 12 mg., seem to be suboptimal.] One of the patients with megaloblastic anaemia of pregnancy had not responded to 80 μg. of vitamin B_{12}, but intramuscular injection of folinic acid produced a satisfactory response.

M. C. G. Israëls

1342. **Megaloblastic Anemia in Pregnancy. Remission following Combined Therapy with Ascorbic Acid and Vitamin B_{12}**
R. G. HOLLY. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **78**, 238–241, Oct., 1951. 6 refs.

The author, from the University of Minnesota Medical School, Minneapolis, reports 5 cases of megaloblastic anaemia associated with pregnancy. The anaemia in 2 patients was refractory to adequate therapy with vitamin B_{12}; one responded subsequently to treatment with folic acid and blood transfusion, and one had a complete remission when ascorbic acid was given with the vitamin B_{12}. Two patients received ascorbic acid only, and one had a minimal reticulocyte response, but on the addition of vitamin B_{12} both had a complete remission. One patient had a spontaneous remission after delivery.

The author discusses the possibility that ascorbic acid deficiency in pregnant women may interfere with the conversion of folic acid to the citrovorum factor, which is the factor lacking in megaloblastic anaemia.

Janet Vaughan

1343. **On the Nature of Castle's Hemopoietic Factor**
S. T. CALLENDER and L. G. LAJTHA. *Blood* [*Blood*] **6**, 1234–1239, Dec., 1951. 7 refs.

The authors describe experiments carried out at the Radcliffe Infirmary, Oxford, in which a marrow-culture technique was used to investigate the nature of Castle's haematopoietic factor. Normal gastric juice (intrinsic factor) and vitamin B_{12} together form a thermolabile haematopoietic factor which ripens megaloblasts *in vitro*, gastric juice and vitamin B_{12} being inactive alone. The haematopoietic factor in normal serum which ripens megaloblasts *in vitro* is also thermolabile, heating to 56° C. for 2 hours destroying some of its activity. In a closely reasoned argument [which should be read by all those interested] the authors discuss the light their observations throw on the interrelationship of haematopoietic factors effective in megaloblastic anaemias, and are led to postulate the existence of an extragastric as well as a gastric source of intrinsic factor.

Janet Vaughan

1344. **Mediterranean Anemia (Hereditary Leptocytosis) in a Chinese Family**
J. H. SILVERBERG and D. SHOTTON. *New England Journal of Medicine* [*New Engl. J. Med.*] **245**, 688–690, Nov. 1, 1951. 1 fig., 11 refs.

1345. **Hereditary Spherocytosis—I. Clinical, Hematologic and Genetic Features in 28 Cases, with Particular Reference to the Osmotic and Mechanical Fragility of Incubated Erythrocytes**
L. E. YOUNG, M. J. IZZO, and R. F. PLATZER. *Blood* [*Blood*] **6**, 1073–1098, Nov., 1951. 7 figs., bibliography.

This is a study of the clinical, haematological, and genetic aspects of hereditary spherocytosis, based on the observation of 28 cases. Essential criteria for the diagnosis of the condition are given as: the presence of spherocytes in the peripheral blood; increased osmotic fragility of the erythrocytes (if the fragility of fresh cells is not significantly increased, determinations should be made after incubation at 37° C. for 24 hours); increased mechanical fragility of fresh erythrocytes; increased autohaemolysis on incubation; a negative antiglobulin reaction; and familial spherocytosis. The erythrocyte abnormality which is the basis of the disease was found to be uninfluenced by splenectomy.

Although the demonstration of spherocytosis in the patient's relations is regarded as necessary for an unequivocal diagnosis, the absence of the trait may be due to gene mutation, low gene penetrance, or possibly illegitimacy. The authors found evidence of low gene penetrance or expression in some of their cases, which they consider stressed the need for still more sensitive laboratory tests in the diagnosis of mild cases of spherocytosis.

Ellis Dresner

1346. **Hereditary Spherocytosis—II. Observations on the Role of the Spleen**
L. E. YOUNG, R. F. PLATZER, D. M. ERVIN, and M. J. IZZO. *Blood* [*Blood*] **6**, 1099–1113, Nov., 1951. 6 figs., 28 refs.

It is well known that splenectomy relieves the haemolytic anaemia in hereditary spherocytosis, although the abnormality of the erythrocytes persists after the operation. The authors, working at the University of Rochester School of Medicine, transfused normal erythrocytes into 3 patients suffering from spherocytosis and, after splenectomy, determined by differential agglutination the proportion of donor's and recipient's erythrocytes in the peripheral blood and in the removed spleens. The spleens contained a significantly higher proportion of abnormal erythrocytes than the peripheral vessels, and whereas the donor's erythrocytes showed practically the same (normal) osmotic fragility whether they were obtained from the periphery or from the minced spleen, the fragility of spherocytes from the spleen was found to be much greater than that of those in venous samples. There was no such differentiation between donor's and recipient's cells in a case of Fanconi's syndrome in which splenectomy was performed, but when spleens removed from patients suffering from non-haemolytic disease were perfused with a mixture of normal erythrocytes and spherocytes, the abnormal cells were selectively trapped in the spleen and histological examination showed them to be in the pulp.

The authors suggest that in spherocytosis the spleen selectively retains the thicker spherocytes and that while these are held in the pulp and removed from the protection of factors present in actively circulating blood, osmotically active substances accumulate within them, causing increased fragility.

H. Lehmann

1347. **The Use of Adrenocorticotropic Hormone and Cortisone in the Treatment of Leukemia and Leukosarcoma**
M. C. ROSENTHAL, R. H. SAUNDERS, L. I. SCHWARTZ, L. ZANNOS, E. P. SANTIAGO, and W. DAMESHEK. *Blood* [*Blood*] **6**, 804–823, Sept., 1951. 5 figs., 23 refs.

The authors have previously reported their early experience of the use of ACTH (corticotrophin) in the treatment of 8 cases of acute and subacute leukaemia (Dameshek *et al.*, *Bull. New Engl. med. Cent.*, 1950, **12**, 11; *Abstracts of World Medicine*, 1950, **8**, 168). They now report the further progress of these patients, together with that of another 34 cases of leukaemia, lymphosarcoma, Hodgkin's disease, and myeloma which have since been treated with ACTH and cortisone with the following results.

Of 15 patients with acute and subacute lymphocytic leukaemia, 3 died during treatment and probably too soon for it to have had any effect, 3 failed to respond at all, and 9 developed remissions of varying degree and duration (1 to 10 weeks), but were little influenced by maintenance therapy. Some of these 9 showed further remission after re-treatment in relapse, but eventually all became refractory to further treatment. Of 5 adults with acute granulocytic leukaemia, 2 failed to respond, 1 showed slight improvement, and 2 were made worse

by the treatment, which resulted in a rapid intensification of the leukaemic process. Two cases of acute monocytic leukaemia failed to show any response to treatment. Of 5 patients with chronic lymphocytic leukaemia improvement was noted in 4, particularly in cases of terminal leukaemia with exfoliative dermatitis or haemolytic anaemia. Some improvement of varying degree was noted in 5 cases of lymphosarcoma, while of the 5 patients with Hodgkin's disease 3 showed improvement in their constitutional symptoms, but there was no fundamental alleviation of the disease itself. Only 1 out of 5 patients with myelomata showed any improvement.

The authors feel that maintenance therapy was beneficial in some cases of lymphosarcoma and chronic lymphocytic leukaemia, while the management of the last stages of Hodgkin's disease was more satisfactory during the administration of ACTH or cortisone. Multiple myelomatosis may be improved for a time by ACTH when other methods have failed. From their observations they feel that ACTH has a stimulating rather than a depressing effect on marrow activity, as judged from the relief of the anaemia, thrombocytopenia, and leucopenia. They consider it is too early yet to make a final estimate of the value of ACTH in the treatment of these types of case. *John F. Wilkinson*

1348. **Radioactive Arsenic in the Treatment of Hodgkin's Disease and of Mycosis Fungoides.** (L'arsenic radioactif dans le traitement de la maladie de Hodgkin et du mycosis fungoïde)
L. MALLETT, G. MARCHAL, and G. DUHAMEL. *Acta Haematologica* [*Acta haemat., Basel*] **7**, 27–38, Jan., 1952. 6 figs., 5 refs.

A radioactive arsenic preparation containing ^{76}As chiefly as sodium arsenate was prepared by neutron bombardment of cacodylic acid in the heavy-water pile at Chatillon sous Bagneux: an activity of 3 to 4 μc. per mg. As was reached. One of the authors had earlier determined that in the guinea-pig the ratio of fixation in different organs of ^{76}As given as this preparation is: intestine, 100; skin, 46; spleen, 25; liver, 17; and adrenal glands, 5·5.

The preparation was given orally, usually in 5 doses of 1 to 2 mg. As at weekly intervals. As might be expected from the intestinal localization found experimentally, vomiting and diarrhoea were the main side-effects. Of 4 cases of cutaneous reticulosis treated, marked improvement of the skin lesions was observed in all. Relapse occurred in 3, but in one, a case of Hodgkin's sarcoma in which the cutaneous element had resisted *x*-irradiation, clinical cure has so far lasted 14 months. The effects of ^{76}As appear to be limited to skin and intestine; spleen and lymph-node reticulosis was not affected.

[Absence of histological data and non-comparability of the photographs reproduced interfere with assessment of these results; but the apparently specific localization suggests that ^{76}As may prove of value in the treatment of the reticuloses, though its long-term results are not likely to differ from those of other agents.]
B. Lennox

1349. **The Use of Radioactive Phosphorus in Treatment of Hodgkin's Disease.** (L'utilisation du phosphore 32 dans quelques cas de maladie de Hodgkin)
R. HUGUENIN, R. SARACINO, and J. GUELFI. *Bulletin de l'Association Française pour l'Étude du Cancer* [*Bull. Ass. franç. Cancer*] **38**, 414–422, 1951. 3 figs., 6 refs.

The results of the treatment of 5 cases of Hodgkin's disease with radioactive phosphorus are described. Accurate assessment of the results is difficult owing to the tendency of the disease to progress irregularly and to its liability to phases of spontaneous regression, but it is considered that the treatment with radioactive phosphorus was far from being without effect. Improvement in the general state of the patient and responses such as lowering of temperature and disappearance of pruritus are ascribed to the treatment. Such responses, however, did not occur in all cases. *L. A. Elson*

1350. **The Rhesus Antibody Anti-E in Pregnancy and Blood Transfusion—I. The Frequency of Occurrence of Pure Anti-E. Report of 12 Cases. II. The Demonstration by Pure Anti-E Serum of Dosage Effect of the Antigen E in the Presence or Absence of the Antigen D**
R. H. MALONE and I. DUNSFORD. *Blood* [*Blood*] **6**, 1135–1146, Nov., 1951. 16 refs.

Since 1945 the authors have examined for Rh antibodies all specimens of blood from Rh-negative multigravidae (and primigravidae with a history of transfusion) submitted for examination to their laboratory at the Blood Transfusion Centre, Sheffield. Between 1945 and September, 1948, they found 3 cases of immunization due to pregnancy or blood transfusion in which anti-E was the only Rh antibody present. Since September, 1948, they have also tested for antibodies the blood of all Rh-positive women with a history suggesting possible immunization. This led to the discovery, in 1949, of 9 further cases of pure anti-E immunization, an incidence of 2·8% of all cases of Rh immunization encountered for the first time during that year, which was considerably higher than could have been expected from previously published figures.

A notable feature of these sera was that they were able to differentiate E/E from E/e erythrocytes on titration, and in 5 of the 10 sera tested this differentiation was present to a very high degree. This is of practical importance for two reasons: (1) anti-e serum is so rare that another means of determining e in the presence of E will be found most useful for the genotyping of the rhesus chromosome; and (2) if an unknown serum is being tested for anti-E, the erythrocytes used should be homozygous, as weak anti-E reactions may occur if only a single dose of the antigen is present.

In the course of experiments on the practical value of anti-E sera in detecting single or double dosage of antigen E, it was found that the presence of the antigen D affected the E antigen–antibody reactions. There were only slight variations in agglutinability when the same anti-E serum was tested against erythrocytes of different individuals of the same genotype, but large differences were seen with cells of different genotypes. The average titration score, calculated according to the method of

Race and Sanger (*Blood Groups in Man*, Oxford, 1950) was four times as high in the case of single E without D as with single E and double D, and nearly twice as high as with single E and single D. Similar effects were seen with anti-e, but were then less noticeable, possibly because of the small quantity of anti-e serum available. There seems thus to exist a quantitative relationship between the agglutination score and the dosage of E and D antigens, as if the score of a particular cell represented the ratio of E to D.

The authors suggest that their results are compatible with the theory of Race and Sanger that there is a limited amount of basic non-specific substance from which the specific antigens are developed by action of the genes. The larger the amount of D produced in a cell, the less would be the amount of C or E; and when C and D are produced—as may be assumed to be the case in sera with single E and double D—the amount of E would be minimal. *H. Lehmann*

1351. **A New Example of the Anti-S Agglutinin**
J. J. VAN LOGHEM, M. VAN DE HART, and J. CORNELIS. *British Medical Journal* [*Brit. med. J.*] **2**, 1383–1384, Dec. 8, 1951. 7 refs.

A patient suffering from a severe chronic anaemia, probably due to osteosclerosis of the bone marrow, received in a period of 14 years 11 blood transfusions, most of them causing mild or severe reactions, and 8 intramuscular injections of whole blood.

In the serum was found, besides complete and incomplete antibodies anti-C and anti-D, a saline-agglutinating antibody of the type anti-S. This agglutinin is apparently of the immune type, because the titre, after administration of 2 intravenous injections of S-positive blood (respectively 20 and 10 ml.) increased from 1 : 4 to 1 : 64, and fell again after the artificial immunization was stopped. The first injection with S-positive blood was followed by a febrile reaction. Rh-negative S-negative blood was well tolerated. No incomplete anti-S antibodies were detected. This is the eighth case in which the anti-S agglutinin was found and the fourth case in which the formation was due to immunization by blood transfusion.—[Authors' summary.]

1352. **" Silent " Erythroblastosis.** (Über die " stillen " Erythroblastosen)
P. LAMERSDORF. *Zentralblatt für Gynäkologie* [*Zbl. Gynäk.*] **73**, 1735–1741, 1951. 2 figs., 10 refs.

According to recent research in Germany 81·5% of the population is Rh-positive and 18·5% Rh-negative. On this basis 11% of all babies from Rh-negative mothers might be expected to be Rh-positive. Only about 1%, however, of all newborn babies show signs of disease attributable to Rh antibodies (Finck). In 2% of those whose blood was antagonistic to the mother's and who were yet clinically healthy, de Vries discovered blood changes indicative of what he termed " silent " erythroblastosis.

In the present critical investigation 20 Rh-positive newborn infants with Rh-negative mothers were compared with 40 newborn infants who had no Rh antagonism with the mother. Only vigorous healthy infants and healthy mothers were examined. A few weeks before the birth the mother's ABO group, Rh reaction, and Rh antibodies were tested. At birth, blood from the cord was similarly investigated, and during the first 20 hours of life, blood from the baby's heel was taken for blood count and haemoglobin estimation (Sahli). Between the 9th and 15th days after birth the Rh-negative women with Rh-positive babies were checked for antibodies. Results of the blood counts are tabulated in two columns, one for first-born children and the other for second and subsequent births. Two graphs are reproduced showing the erythroblast cell counts from babies during the first 3 or 4 days of life.

It was found that 19 newborn infants showed ABO antagonism to their mothers. Of these, 3 cases were of A–B antagonism and 3 others antagonism between A or B and AB. The blood smears differed in no way from the others. It is considered of special interest that where ABO antagonism existed in these two categories it was more common in later babies than in the first-born, in the ratio of 4 to 1. The babies with Rh antagonism showed slight changes indicating a low-grade haemolytic anaemia; no antibodies were found in the blood of these infants. In only one mother where there was Rh antagonism were antibodies found in the blood. On the 13th day post partum the titre was 1 in 8 against R_1r and 1 in 16 against R_1R_1. The blood smear of the baby was normal. *E. W. Kirk*

1353. **Separation, Concentration, and Transfusion of Platelets**
G. H. L. DILLARD, G. BRECHER, and E. P. CRONKITE. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **78**, 796–799, Dec., 1951. 4 refs.

In experiments carried out at the U.S. Naval Research Institute, human blood and blood from dogs and guinea-pigs was collected through plastic tubing into 200-ml. siliconed bottles containing 20 ml. of a solution of ethylene diamine quadri-acetate (" sequesterene Na_2 "), 1%, and sodium chloride, 0·7%, in distilled water and immediately centrifuged at $30 \times g$ for 50 minutes at 5° C. The supernatant plasma containing the platelets was siphoned through siliconed apparatus into another siliconed tube and then centrifuged for the same time at 10 times the previous rate. This left the platelets as a loosely packed mass which could be re-suspended in an aliquot of the supernatant plasma.

Transfusions of this suspension were given within 4 to 5 hours of collecting the blood to guinea-pigs and dogs. Using Brecker and Cronkite's method of platelet counting (*J. appl. Physiol.*, 1950, **3**, 365), the authors showed that the platelets survived *in vivo*, reversed coagulation defects, and prevented haemorrhage. In sequesterene there was no tendency for the platelets to become sticky, agglutinate rapidly, or undergo morphological changes, whereas other anticoagulants, including a standard citrate–citric-acid–dextrose mixture, and passage through a cation-exchange-resin column were found unsatisfactory. *I. Dunsford*

Respiratory Disorders

1354. **Green Sputum**
A. J. ROBERTSON. *Lancet* [*Lancet*] **1**, 12–15, Jan. 5, 1952. 6 figs., 21 refs.

Green sputum has been ascribed to various causes in the past. Andral in 1821 explained it as depending on the quantity of blood contained in the sputum. Laennec in 1834 agreed with this view, but Grisolle (1841) could not satisfy himself that blood was responsible. Traube's views (1864) were summarized as follows by Nothnagel: the colour may be due to jaundice together with respiratory infection; or to chronic unresolved pneumonia or lung abscess; or to subacute pneumonia, either tuberculous or otherwise.

The present author describes his method of obtaining a green solution from sputum. He shows that the colouring matter gives the absorption spectrum of verdoperoxidase (also called myeloperoxidase), an enzyme present in the structure of the granulocyte. It is suggested that failure to excrete verdoperoxidase set free from disintegrating granulocytes results in its accumulation in stagnating sputum within the body. The causes of green sputum are classified as follows: (1) stagnation of purulent sputum with poor excretion of verdoperoxidase—as in bronchiectasis, lung abscess, and inhalation pneumonia; (2) bacterial contamination of sputum outside or inside the body by *Pseudomonas aeruginosa*; and (3) severe jaundice, especially with broncho-biliary failure. *John Anderson*

1355. **Terramycin Therapy of Pneumonia: Clinical and Bacteriologic Studies in 91 Cases**
G. G. JACKSON, T. H. HAIGHT, E. H. KASS, C. R. WOMACK, T. M. GOCKE, and M. FINLAND. *Annals of Internal Medicine* [*Ann. intern. Med.*] **35**, 1175–1202, Dec., 1951. 4 figs., 18 refs.

In this paper is reported a study of 91 patients with pneumonia treated with terramycin at the Boston City Hospital, Massachusetts. Pneumococci were isolated from the sputum in 68 cases, 16 of which had positive blood cultures. The remaining 23 cases included 4 of primary atypical pneumonia, the rest being regarded as cases of bacterial pneumonia; included in these were infections by β-haemolytic streptococci, *Haemophilus influenzae*, and *Staphylococcus aureus* (haemolytic and coagulase-positive). Patients' ages ranged from 16 to 89 years, and males predominated among patients with the pneumococcal type of infection. Of the predisposing causes chronic alcoholism and bronchopulmonary infections were significant. A single starting dose of 1·0 g. terramycin orally was followed by 0·5 g. 4- to 6-hourly, reaching a total of 10 to 30 g. in 4 to 10 days. Terramycin was effective in pneumococcal pneumonia and favourable in other bacterial and primary atypical pneumonias. In cases in which the lungs cleared more slowly it was observed that the flora of the sputum had been replaced by staphylococci, which also appeared in the stools of some of the patients who developed diarrhoea, necessitating the use of aureomycin. Gastro-intestinal symptoms, such as nausea, vomiting, or diarrhoea, were frequent toxic effects; drug rash, stomatitis and glossitis, and nitrogen retention occurred less frequently. In 5 of the 7 patients who died, toxic effects of terramycin on the gastro-intestinal tract may have largely contributed to the fatal outcome, and in 4 of these patients staphylococci played an important pathogenic role in the lungs. *I. Ansell*

1356. **The Management of Lung Abscess, with Special Reference to the Place of Antibiotics in Therapy**
E. H. DRAKE and F. M. SONES. *Annals of Internal Medicine* [*Ann. intern. Med.*] **35**, 1218–1236, Dec., 1951. 10 figs., 15 refs.

In this paper from the Henry Ford Hospital, Detroit, Michigan, are analysed the results of therapy in 45 proved cases of lung abscess in the past 10 years. The authors note the usual pathological mechanisms, such as bronchial obstruction with resulting atelectasis, infection, and impaired blood supply to the involved segment. They stress the importance of a history of recent loss of consciousness and impaired normal physiological mechanisms, as well as associated upper respiratory infection, diabetes, alcoholism, or heart disease. Haemoptysis and localized chest pain are emphasized as symptoms.

In the series described physical signs varied with the underlying pathology. Radiology and bronchoscopy were most useful in the location of abscesses, 65% of which occurred in the upper lobe, with a greater frequency on the right side. Cases were divided into 33 "putrid" and 12 "non-putrid"—spirochaetes, fusiform bacilli, *Micrococcus catarrhalis*, and non-haemolytic streptococci being more common in the former. This differentiation was regarded as dependent more upon the mechanics of drainage than on any basic aetiological difference.

Crystalline penicillin, 100,000 units intramuscularly every three hours, was found most useful, and was supplemented by aerosol therapy when impaired blood supply was suspected. Used in the "pre-abscess" stage, penicillin aborted cavity formation. When adequate drainage did not occur spontaneously or could not be induced by postural or bronchoscopic means surgical intervention was advised, especially when progress radiographs failed to reveal consistent diminution in cavity size. Even if the advance of the lesion had apparently been stopped, reduction of functional efficiency of the involved segment was likely to occur after 6 weeks owing to development of fibrosis and bronchiectasis. In such cases the authors consider that lobectomy may become more popular. *I. Ansell*

Genito-urinary Disorders

1357. **Nephrotic Syndrome Treated with Intravenous Dextran**

P. D. Bedford and P. M. G. Broughton. *Lancet* [*Lancet*] **2**, 1161–1163, Dec. 22, 1951. 14 refs.

Salt-free dextran given intravenously to a patient with nephrotic oedema had no effect on his clinical condition. Dextran produced an immediate increase of about 30% in the blood volume, with no symptoms or signs of circulatory overloading. No diuresis resulted from this haemodilution. No dextran was detected in the oedema fluid during and after the injections or in tissues examined post mortem two months after the last infusion.—[Authors' summary.]

1358. **Norepinephrine and Epinephrine Effect on Renal Hemodynamics. With Particular Reference to the Possibility of Vascular Shunting and Decreasing the Active Glomeruli**

J. H. Moyer and C. A. Handley. *Circulation* [*Circulation*] **5**, 91–97, Jan., 1952. 1 fig., 19 refs.

The authors have studied the renal haemodynamic effect of continuous infusions of noradrenaline and adrenaline in dogs. By means of the technique of renal-vein catheterization, the renal extraction of creatinine and anterior pituitary hormone were determined and renal plasma flow (R.P.F.) calculated. The glomerular filtration rate (G.F.R.) was determined as the creatinine clearance, and the maximum tubular reabsorptive capacity for glucose (T.M.G.) was also measured. Two groups of female dogs were studied; one group of 9 animals received a constant infusion of 1 in 100,000 adrenaline, and the second group, of 7, a constant infusion of noradrenaline of the same strength.

During control periods, the values for G.F.R., R.P.F., and T.M.G. were within normal limits. After infusion the R.P.F. decreased progressively and in inverse proportion to the rise in blood pressure. At first, the G.F.R. was virtually unchanged, so that an increased filtration fraction resulted. With further decrease in the R.P.F. the G.F.R. declined steadily, its decrease being accompanied by a parallel reduction in urine volume. At the point where renal function was severely depressed, T.M.G., R.P.F., and G.F.R. all showed the same order of decrease.

Imidazoline hydrochloride was given to 7 dogs—to 5 before the infusion of adrenaline, and to 2 before noradrenaline. The effects of noradrenaline on the blood pressure and renal function were completely blocked; but when adrenaline was given, marked hypotension occurred (adrenaline reversal). In 2 of these 5 dogs the fall in blood pressure was too great to permit accurate renal studies, but in the other 3 the G.F.R. fell about 50%, although the R.P.F. did not change significantly.

The authors consider that the decrease in R.P.F. and increase in filtration fraction occurring before other changes in renal function and indicating efferent arteriolar constriction, followed by parallel reduction in both T.M.G. and G.F.R., suggests a decrease in the number of active nephrons. They conclude that under the conditions of this experiment, active nephrons can be excluded from the renal circulation, that this exclusion can be prevented by adrenergic blocking drugs, but that there is no evidence that adrenaline or noradrenaline activates renal vascular shunts in dogs. *J. F. Goodwin*

1359. **Observations on the Fanconi Syndrome and Renal Hyperchloraemic Acidosis in the Adult**

M. D. Milne, S. W. Stanbury, and A. E. Thomson. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **21**, 61–82, Jan., 1952. 3 figs., bibliography.

Two adult cases of renal tubular insufficiency are described and compared. One was a typical case of hyperchloraemic renal acidosis; the other was a case of the Fanconi syndrome with hyperchloraemic acidosis. Each presented with osteomalacia and multiple pseudo-fractures, and in both cases continued loss of potassium in the urine resulted in a low serum-potassium, and paralytic attacks similar to those of familial periodic paralysis. In both cases the plasma chloride concentration was increased, and the alkali reserve low; but, in spite of a severe degree of systemic acidosis, the urine reaction was invariably neutral or only faintly acid.

The patient with hyperchloraemic acidosis showed no evidence of an associated glomerular insufficiency, while the patient with the Fanconi syndrome had reduced renal clearances of inulin, creatinine, and urea. Both showed subjective and objective improvement in the osteomalacia on identical treatment with calciferol and sodium and potassium citrate. The more severe renal defect in the latter patient, however, led to greater difficulty in control: hypercalcaemia, alkalosis, and oedema each developed in the course of treatment. The control of therapy and the prognosis in each case are discussed.

The excretion of electrolytes and reasons for excessive loss of fixed base in the Fanconi syndrome are described in detail, and the causation of osteomalacia is discussed. In both cases there was defective absorption of bicarbonate in the renal tubule. The Fanconi syndrome showed additional defects in the reabsorption of glucose, aminoacids, and acetoacetic acid. Reasons are given for the belief that abnormally high phosphate excretion in these cases is not due to a specific tubular reabsorptive defect, but is secondary to some extrarenal influence. A combination of secondary hyperparathyroidism and of systemic acidosis is suggested as the possible causative factor.

It is suggested that the high urinary ammonia coefficient in the Fanconi syndrome, and the absence of complicating nephrocalcinosis in such cases, may be attributable to organic-aciduria.—[Authors' summary.]

Endocrine Disorders

1360. **Splenic Arteriovenous Differences in Blood Cells during the Hematologic Reaction to Adrenal Cortical Stimulation**

D. H. SOLOMON and S. R. HUMPHREYS. *Blood* [*Blood*] **6**, 825–831, Sept., 1951. 10 refs.

The authors, in experiments carried out at the National Heart Institute, Baltimore, Maryland, studied the differences in the eosinophil content of blood from the splenic vein and femoral artery of the intact dog following the administration of ACTH (corticotrophin) or adrenaline in an attempt to determine the relationship of splenic function to the eosinophil count in the circulating blood. In no case was there a significant net increase in the eosinophil content of the spleen, but in 3 out of 7 experiments with adrenaline and in one with ACTH there was a significant splenic output of eosinophils. There were no significant differences in the haematocrit determinations, and arterio-venous differences in neutrophil count observed were quite independent of those in the eosinophil count simultaneously determined.

The authors conclude that the spleen does not significantly retain or destroy eosinophils during the development of eosinopenia on stimulation of the adrenal cortex. On the other hand, as under certain conditions eosinophils were expelled into the general circulation when other factors were causing eosinopenia, it appears possible that the spleen may be capable of storing cells of one type and releasing others into the circulation.

John F. Wilkinson

1361. **Influence of ACTH and Cortisone on Dermal Spread. Suppressed Action of Hyaluronidase due to Connective-tissue Changes**

G. ASBOE-HANSEN. *Acta Endocrinologica* (*Copenhagen*) [*Acta endocrinol., Kbh.*] **9**, 29–36, Jan., 1952. 1 fig., 14 refs.

The author reviews the literature on the effects of hormones on dermal spread, with particular reference to their inhibitory action on hyaluronidase. His own investigations were carried out on 30 white rabbits, half of which were given 15 i.u. of ACTH subcutaneously in two doses daily for 5 days, and the remainder 50 mg. of cortisone subcutaneously in two doses daily, also for 5 days. The spreading experiments were performed before the hormones were given, and also 2 hours after the ninth injection, 0·1 ml. of normal saline being injected into the left flank and an equal volume containing a standardized solution of hyaluronidase into the right flank. After the first hour an equal volume of Evans blue or indian ink was injected into both sides; 24 hours later the areas were traced and measured with a planimeter.

The results are tabulated and show that the hyaluronidase spread was reduced in the animals receiving ACTH and cortisone, while in the controls the spread was increased in all by cortisone, and in most of them by ACTH. Earlier work had shown that ACTH and cortisone reduce the dermal hyaluronic acid content, so that the hyaluronidase would have less substrate on which to act, with a resultant decrease in spread. In the absence of hyaluronidase, the hormones having increased dermal permeability by their action on hyaluronic acid, there would be an increase in spread. The lack of consistency of ACTH in this respect is to be studied further. It was concluded that there was no direct inhibition by the hormones of the enzyme hyaluronidase, a fact which has been confirmed *in vitro*.

R. St. J. Buxton

1362. **Effect of Cortisone, Related Hormones, and Adrenalectomy on Susceptibility of Mice to Virus Infections**

C. M. SOUTHAM and V. I. BABCOCK. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **78**, 105–109, Oct., 1951. 12 refs.

Mice treated with 2·5 mg. of cortisone daily for 5 or more days were consistently rendered more susceptible to West Nile, Ilheus, and Bunyamwera viruses given at least 36 hours after the start of treatment. ACTH in a dosage of 0·5 mg. every 6 hours for 5 days had no effect on their susceptibility to West Nile or Ilheus viruses. When 4 mg. in gelatin was given every 12 hours there was evidence of increased susceptibility. Adrenalectomy, testosterone, oestradiol, progesterone, and deoxycortone had no effect.

In a trial on 4 human patients receiving cortisone treatment (400 mg. intramuscularly every 12 hours in 3; 200 mg. by mouth every 6 hours in 1), West Nile virus was given 2 to 4 days after the start of treatment, but there was no indication that they were more susceptible than were 18 similar patients who received this virus in the absence of cortisone or ACTH therapy.

R. Hare

1363. **The Use of Radioactive Iodine in the Assessment of Thyroid Function**

J. F. GOODWIN, A. G. MACGREGOR, H. MILLER, and E. J. WAYNE. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **20**, 353–387, Oct., 1951. 9 figs., 48 refs.

The authors report from Sheffield on the use of radioactive iodine in the assessment of thyroid function. They point out that ^{131}I is now the standard isotope used for investigation. Fundamental facts generally accepted are that the thyroid can concentrate inorganic iodine to 10,000 times the blood level; that it is excreted by the kidney in proportion to the blood level, and also in faeces, air, and sweat. Attempts have been made to find a means whereby ^{131}I can be used to differentiate clearly between various groups of thyroid abnormalities. The disadvantages of some tests generally used are described. The authors observe that since thyrotoxicosis

may be due to an increase in blood thyroxine level, its measurement may be of help in diagnosing the doubtful case.

In the present series all 96 patients—16 of whom had normal thyroid function and the rest various types of thyroid disease or thyrotoxicosis-simulating diseases—underwent routine tests before ^{131}I was given. The method of administration and the type of counter used are described. The counting centre was taken as 2 cm. below the skin over the thyroid isthmus. Since the estimated gland dose is 35 r following a 25-μc. dose it is considered wiser to perform the test once only.

Tables showing the results of all the investigations on every patient are given. In common with other authorities the authors did not find the basal metabolic rate to be proportional to the degree of toxicity. Although the clinical degree of toxicity corresponded to the peak 24-hour uptake, there was overlapping between results in the intermediate groups and those in the toxic and non-toxic cases. A similar lack of clear distinction between the groups was found in the 24-hour urinary excretion and thyroid clearance levels.

The only test which clearly demarcated between cases with normal thyroid function and the toxic and intermediate cases was estimation of the 48-hour level of protein-bound iodine. In view of the accuracy and sensitivity of the test it is suggested as a useful aid to diagnosis even in the out-patient department.

V. M. Dalley

1364. **Production of Experimental Cretinism in Dogs by the Administration of Radioactive Iodine**
C. A. Smith, H. A. Oberhelman, E. H. Storer, E. R. Woodward, and L. R. Dragstedt. *Archives of Surgery* [*Arch. Surg., Chicago*] **63**, 807–820, Dec., 1951. 12 figs., 11 refs.

In the Department of Surgery of the University of Chicago the authors have studied cretinism in dogs produced by the administration of radioactive iodine (^{131}I) to puppies shortly after birth, or to pregnant bitches near term so as to produce cretinism in the offspring by destruction of the thyroid gland. When ^{131}I was given to puppies, litter mates were kept as controls. Observations were made on physical changes, growth, and bone development, and on the blood with particular reference to the serum cholesterol and lipid levels. Thyroid function was assessed by the conversion ratio of free to protein-bound iodine following administration of ^{131}I. It has been shown that when the protein-bound fraction contains less than 10% of the total blood iodine content hypothyroidism is present. Puppies were given ^{131}I subcutaneously at varying ages and intervals, total doses ranging from 1·5 to 5 mc. Bitches received about 15 mc. from 4 to 10 days before whelping.

The progress of the treated puppies was fairly constant, and they showed similar radiological, biochemical, and pathological changes. They were stunted, pot-bellied, and lethargic, with coarse hair growing from thickened skin. Prognathism and macroglossia were noted. The serum cholesterol and lipid levels were increased. Radiographs showed that ossification centres were delayed, and when present were smaller than normal; the long bones were comparatively shorter in the treated animals. At necropsy virtual absence of thyroid tissue, with enlargement of the pituitary, was demonstrated. Parathyroid and other endocrine glands were normal. There was delay in the ossification of the cartilaginous bone, blurring of the osteoid line at the epiphyses, and marked increase in the subcutaneous fat. That ^{131}I passes the placental barrier was shown by the production of cretinism in the entire litter of the treated bitches. The pups fed poorly and there was a high neonatal mortality. The cretinism was in all respects like that produced after birth.

J. N. Harris-Jones

1365. **The Effect of Smoking on Hyperthyroidism**
E. C. Bartels and J. J. Coll. *Lahey Clinic Bulletin* [*Lahey Clin. Bull.*] **7**, 167–172, Oct., 1951. 2 figs., 9 refs.

The effects on blood pressure, pulse, and basal metabolic rate (B.M.R.) of smoking 2 cigarettes were studied in 21 hyperthyroid subjects. The B.M.R. rose 3·5% to 23% (average 8%) in 13, was unchanged in 5, and fell 3% to 9% in 3; the systolic blood pressure rose by an average of 15 mm. Hg in 11 subjects and was unchanged in the remainder; and the pulse rate increased by an average of 15 beats per minute in 16 subjects. These observations were repeated in 6 subjects after their hyperthyroidism had been controlled with antithyroid drugs; no essential alteration in response was noted. Although no evidence is forthcoming that hyperthyroid patients are more sensitive than normal individuals to tobacco, it is felt that the rise in B.M.R. and pulse rate which so frequently occurs justifies the prohibition of smoking during treatment.

[It is not indicated whether the subjects studied were or were not heavy smokers, a factor which might be expected to influence at least some of the observations.]

H. McC. Giles

1366. **Final Cure of Thyrotoxicosis by Prolonged Administration of Iodine.** (Guérison sans récidive de la maladie de Basedow par l'emploi continu de l'iode)
M. Yener. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **27**, 3548–3550, Dec. 2, 1951.

Since 1930 the author, who is professor in the Faculty of Medicine of Istanbul, has treated some 60 cases of thyrotoxicosis by prolonged administration of iodine. Every patient received a standard dose of 20 drops twice daily of the following solution: iodine 0·2 g., potassium iodide 2 g., water 20 ml.; this was continued uninterruptedly for periods up to 5 or 6 years. Brief reports are given of 7 successfully treated cases. No relapses have been observed during a follow-up period extending, in some instances, to 9 or 10 years. [In most of the cases, however, no indication is given of the length of the follow-up period, and only 20 patients out of 60 remain under the author's observation. The value of this treatment cannot be assessed on the scanty data provided.]

H. McC. Giles

See also Pathology, Abstract 1201.

Diseases of the Skin

1367. **Occupational Dermatoses in Physicians**
E. EPSTEIN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1751–1754, Dec. 29, 1951.

In view of the fact that physicians are exposed to many irritating chemicals and infections in their professional work, a questionnaire was sent to 75 dermatologists requesting information on the incidence of dermatoses in physicians under their care; 60 (80%) replied.

Contact dermatitis was the commonest condition reported. Mechanical trauma in scrubbing-up was the commonest cause of dermatitis of the hands, and although reduction of scrubbing time by the use of agents such as hexachlorophene prevented many cases of dermatitis, they were sometimes themselves responsible for sensitization. Mercurial antiseptics and formaldehyde (in pathologists) were frequent causes, as also were orris root used in certain glove powders and the rubber gloves themselves. Of local analgesics procaine was the commonest sensitizing agent, and of antibiotics penicillin was incriminated 5 times as often as streptomycin. However, self-medication was claimed to be a commoner cause of contact dermatitis in physicians than was occupational exposure.

Of infections, impetigo and furunculosis were the commonest, but dermatophytids were no commoner in physicians than in the general population. Parasitic infestations were uncommon, but 4 dermatologists had caught scabies from patients, and 8 thought they had been infected by patients with warts. Although, in the author's view, accidental syphilitic infection is rare, 16 contributors reported a total of 27 extragenital chancres in physicians. On the other hand, 22 contributors (40%) stated that they had never seen any kind of skin infection passed to a physician by a patient.

Radiodermatitis is the most serious skin disease found in physicians. Although efficient means of protection are available, too many cases still occur as the result of ignorance and carelessness. Injuries such as cuts at operations or burns from electrical appliances were uncommon. The author feels that more could be done by medical schools to teach students the importance of protecting themselves against occupational skin diseases.
Stephen G. Gang

1368. **Exfoliative Dermatitis Associated with Liver Changes and Hypoproteinaemia**
J. S. PEGUM. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **100**, 304–318, 1951. 5 figs., 14 refs.

In this paper 3 cases of generalized dermatitis are described. The first was in a man aged 65 who died after an illness of 2 years' duration, beginning with exfoliative dermatitis and ending with continued oedema, ascites, wasting, anaemia, and achlorhydria. During the course of the disease protein loss from the skin was estimated to be between 27 and 14 g. daily; the plasma protein level was approximately 4 g. per 100 ml. Liver biopsy revealed perilobular fatty infiltration, and at necropsy areas of focal necrosis were found. The second patient had suffered from exfoliative dermatitis for 3 months; liver biopsy showed perilobular fatty infiltration, the plasma protein level was 4·5 to 6·2 g. per 100 ml., and oedema was present in moderate degree. In both these patients it is presumed that the loss of protein in the scales from the skin was sufficient to produce the hypoproteinaemia and oedema. The fatty changes in the liver were considered of doubtful significance, but in the first case they were severe enough to be regarded as playing a large part in causing death, even though results of liver function tests were normal. The interest of these 2 cases lay in the severity of the protein loss from the skin.

The third case presented no special features, being one of erythrodermia in which there was no hypoproteinaemia or loss of protein from the skin and no histological changes as seen on liver biopsy. *Thomas Hunt*

1369. **Clinical Evaluation of " Diphenylpyraline " as an Antifungal Agent**
O. SOKOLOFF. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **64**, 754–756, Dec., 1951. 1 ref.

On 103 patients with various fungus infections a therapeutic trial was carried out with 2% " diphenylpyraline " (1-methyl-piperidyl-4-benzhydryl ether), either as a lotion or in a standard ointment base. Except in one case there were no irritant effects or signs of sensitization. Apparently dramatic results were obtained in tinea pedis, but " fully established conclusions require further corroboration ". *E. W. Prosser Thomas*

1370. **Clinical and Mycological Observations on an Epidemic of Trichophytosis Transmitted to Man from the Rabbit.** (Observations cliniques et mycologiques sur une épidémie de trichophytie transmise du lapin à l'homme)
X. VILANOVA and M. CASANOVAS. *Presse Médicale* [*Pr. méd.*] **59**, 1760–1762, Dec. 25, 1951. 8 figs.

There have been a considerable number of instances in Barcelona in which ringworm of rabbits has been transmitted to man. Such infection has usually occurred in those who handled infected rabbits or children who played with them. On the glabrous skin the lesions have been of typical nummular and circinate type, usually multiple, with much inflammation and often containing pustules. When the scalp was infected there was much desquamation with some loss of hair; sometimes a kerion formed. In the rabbit the disorder always appeared first on the snout and then spread. There was extensive scaling, but no inflammation. In both man and the rabbit the fungus could be found easily in the scales. The organism grew readily when cultured on the usual media, and was found to be *Trichophyton mentagrophytes*. In all the authors' cases the trichophytin test was strongly positive. *E. Lipman Cohen*

1371. **Nodular Cutaneous Elastidosis with Cysts and Comedones.** (L'élastéidose cutanée nodulaire à kystes et à comédons)
M. FAVRE and J. RACOUCHOT. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **78**, 681–702, Nov.–Dec., 1951. 10 figs., 6 refs.

This is a clinical and histological study of a condition which the authors consider to be far from rare and to possess concise characteristics. Sites of election are the temporal and periorbital regions, ears, and nape of neck. The lesions consist of nodules and comedones, often thickly distributed; comedones are generally situated in the nodules, which are elevated, firm, yellowish, and appear translucent; some resemble colloid milia. In the nodules the pilo-sebaceous systems are so altered as to give the appearance of a polycystic skin. [Alterations of the pilo-sebaceous system are not mentioned in descriptions of colloid milia.] The walls of the pilar sacs frequently grow out into the dermis. The sweat glands also sometimes become cystic. The dermis is sclerotic, and there is atrophy of the sebaceous glands.

The degenerated tissue of the upper dermis takes elastic-tissue stains, but the authors draw no conclusions as to the nature of the degeneration and propose to qualify it by the term " elastidosis ".

James Marshall

1372. **Circumscribed Cutaneous Aplasia of the Vertex.** (Aplasie cutanée circonscrite du vertex)
D. ARGÜELLES-CASALS. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **78**, 728–729, Nov.–Dec., 1951. 1 fig.

The author presents a brief review of the literature on this rare condition and reports a case. A white Cuban girl aged 16 had an atrophic, cicatricial, and hairless patch 3 cm. by 1 cm. on the vertex. The lesion had been present since birth, and was noted when a benign papilloma developed on it. There were no other malformations or defects, and the parents were not similarly affected.

James Marshall

1373. **Treatment of Lupus Erythematosus with Vitamin B_{12}. Preliminary Report of 4 Cases**
S. GOLDBLATT. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **17**, 303–304, Dec., 1951. 2 refs.

The author reports the effects of vitamin B_{12} in 3 cases of chronic and one case of subacute disseminated lupus erythematosus. One patient with chronic discoid lupus erythematosus of recent origin diagnosed on histological and haematological grounds regressed and was free of lesions in 8 weeks. The other 2 cases were of long standing. The patients had had previous treatment, including heavy-metal, liver, and tocopherol therapy, but suffered many recurrences. They responded well to vitamin B_{12}, but the response was less dramatic than in the first case. The dosage of vitamin B_{12} in the above 3 cases was 15 μg. weekly given intramuscularly. The fourth case, a severe one of subacute disseminated lupus erythematosus, was clinically atypical, but was finally diagnosed on biopsy. The patient was markedly photosensitive, exposure to sunlight provoking an explosive eruption on one occasion before treatment. Treatment was with 15 μg. of vitamin B_{12} 3 times weekly. It is noted that the patient became pregnant a month before treatment was started. Exposure to sunlight during treatment provoked a mild reaction, which faded quickly. When last examined the patient was still under treatment (and still pregnant), but the lesions had almost disappeared.

The author considers that his results justify a more extended trial of vitamin B_{12} in lupus erythematosus. He points out that the vitamin has been found non-toxic in doses of 5,000 μg.

William Hughes

1374. **Effect of " Aminopterin " on Epithelial Tissues**
R. GUBNER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **64**, 688–699, Dec., 1951. 3 figs., 34 refs.

Experimental and clinical studies with aminopterin and other folic acid antagonists have shown that they inhibit cellular proliferation in tissue derived from mesenchyme. The present investigation suggests that aminopterin also has an inhibitory effect on epithelial structures; wound healing and epithelial growth are affected, alopecia may occur, and there may be atrophy and ulceration of mucous membranes.

Psoriasis was improved in 13 patients by treatment with aminopterin. The dose used was 1·5 to 2·0 mg. daily (total, 14 to 140 mg.). In 7 cases there was associated arthritis, and in these the response was best. After a course of 14 to 28 mg., treatment was interrupted in most cases on account of toxic effects (ulceration of the buccal mucosa, alopecia, and delay in wound healing).

S. T. Anning

1375. **Microsporosis of the Scalp. Evaluation of a New Therapeutic Agent**
B. APPEL, M. J. TYE, W. HALPERN, and D. PACI. *New England Journal of Medicine* [*New Engl. J. Med.*] **245**, 1003–1006, Dec. 27, 1951. 1 fig., 5 refs.

Asterol dihydrochloride, a new antifungoid preparation, in 2% water-soluble ointment and 2% tincture was used at the Boston City Hospital in direct-action tests *in vitro* and in a clinical study of 61 children with microsporon capitis, 16 of whom were infected with *Microsporon canis* and 45 with *M. audouini*. The diagnosis was confirmed in each instance by mycological examination, direct microscopical examination, and culture. The tincture was found to be more effective than the ointment *in vitro*. Although the studies were incomplete and the period of observation too short the authors conclude that the drug merits further observation.

G. B. Mitchell-Heggs

1376. **Treatment of Alopecia Areata Totalis and Universalis with Cortisone Acetate**
C. J. DILLAHA and S. ROTHMAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **18**, 5–6, Jan., 1952. 5 refs.

Three of four patients with alopecia areata, varying from almost total to universal, experienced a regrowth of hair detectable after one month of therapy with oral cortisone acetate.—[Authors' summary.]

Disorders of the Locomotor System

1377. **The Anti-rheumatic Effects of 3-Hydroxy-2-phenylcinchoninic Acid (HPC) in Gout, Rheumatic Fever, and Rheumatoid Arthritis**
J. SIMSON and J. J. BUNIM. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **222**, 523–529, Nov., 1951. 1 ref.

The authors report the results of a clinical trial carried out at Bellevue Hospital, New York, of 3-hydroxy-2-phenylcinchoninic acid (HPC) in the treatment of 10 cases of rheumatoid arthritis and 6 of rheumatic fever, confirming the findings of Blaushard *et al.* (*Bull. Johns Hopk. Hosp.*, 1950, **87**, 50), and in addition record the treatment of 5 cases of gouty arthritis with this drug. HPC was given in a daily dosage of 20 to 40 mg. per kg. body weight divided into 3 doses preferably given after meals. The total dose ranged from 5·4 g. to 81·4 g.

The results of treatment in gout were very satisfactory, and the drug is considered useful in this condition, especially where there is intolerance of, or resistance to, colchicine. Results in rheumatic fever and rheumatoid arthritis were comparable to those achieved with adequate salicylate therapy. One or more toxic reactions occurred in 16 out of the 21 cases, and 4 cases relapsed on discontinuing treatment. Toxic manifestations included frequency of micturition, dysuria, nocturia, impairment of renal function, nausea, vomiting, diarrhoea, erythema, vesiculation, pruritus, menstrual delay, paraesthesiae, and bradycardia. *Harry Coke*

1378. **Myositis Ossificans Progressiva**
H. D. RILEY and A. CHRISTIE. *Pediatrics* [*Pediatrics*] **8**, 753–767, Dec., 1951. 14 figs., 16 refs.

In this paper 4 cases of myositis ossificans progressiva are recorded from Nashville, Tennessee. Cortisone was tried in 2 cases, with beneficial results in one.

The first patient was a 15-month-old boy. A mass had been noticed over the occiput when he was 3 months of age; subsequently more masses developed over the body and became stony hard. Early radiographs showed no calcification, but as the disease advanced this became increasingly apparent. There was no family history of similar disease and no history of previous trauma. The child lay stiffly and could not sit alone; the arms were almost fixed owing to axillary calcification. The patient was given 2 small blood transfusions to correct a mild anaemia before cortisone therapy was started in a dosage of 10 mg. 6-hourly. The eosinophil count fell from 200–300 per c.mm. to 30–75 per c.mm. By the 3rd day the child's disposition had improved, and by the 8th day he could sit alone and reach for food. Improvement continued. On the 14th day cortisone was reduced to 10 mg. daily with no recurrence of rigidity. The patient was discharged on this daily dose; by this time he could feed himself. During a 10-month follow-up period the improvement was maintained, but one more mass developed.

The second case was in a girl of 16 years, the disease having first been noted when she was 2 months old. Cortisone, 125 mg. daily, was given in this case also, but there was no improvement.

The third patient was first seen at 18 months of age, when microdactylia and hallux valgus were noted. Cortisone therapy was not tried in this case, and deep *x*-ray therapy failed to improve the condition.

In the last case the patient, a girl, was 12 years old when seen in 1935, and had had the disease for 5 years. There were many hard masses in the trunk and limbs and great limitation of movement. Radiological examination showed calcification among the spinal muscle masses; microdactylia and hallux valgus were also present. The patient in this case did not report back and was not followed up.

The aetiology, pathology, diagnosis, and treatment of myositis ossificans progressiva are discussed. It is shown that the pathological picture is one of calcification of the connective tissue between the muscles, and not of the muscle itself. The early case which improved with treatment suggests that the disease may be related to disturbed steroid metabolism. *A. T. MacQueen*

1379. **Hepatogenous Osteoporosis.** (Hepatogene Osteoporosen)
U. COCCHI. *Radiologia Clinica* [*Radiol. clin., Basel*] **20**, 362–382, Nov., 1951. 4 figs., bibliography.

Clinical reports on osteoporosis in association with chronic diseases of the liver are very uncommon, probably because the association is not suspected and therefore not investigated.

The author reports 27 cases of osteoporosis seen in patients with cirrhosis, acute yellow atrophy, obstructive jaundice, and external biliary fistulae. Histologically the bones showed simple osteoblastic or osteoclastic osteoporosis. There was some evidence of defective vitamin-D absorption, and of endocrine disturbance in some cases. It is suggested that cirrhosis of the liver and similar degenerative maladies interfere with the absorption of calcium, fat, and phosphorus and thus promote osteoporosis. *G. F. Walker*

ACUTE RHEUMATISM

1380. **Rheumatism of the Central Nervous System.** (Reumatizam centralnog nervnog sistema)
M. KNEŽEVIČ. *Liječnički Vjesnik* [*Liječn. Vjesn.*] **73**, 249–255, Nov., 1951. 8 figs., 20 refs.

Out of approximately 1,500 necropsies on rheumatic subjects performed at Vrapče, Croatia, definite changes in the brain were found in 26, in all of which rheumatic lesions were also found in other organs. Details of the post-mortem findings in these 26, cerebral and otherwise,

are given. Macroscopic thickening of the leptomeninges, especially in the region of the basal cisterns, was present in all cases, but the most marked inflammatory changes occurred in the choroid plexus, where in 19 subjects large or small centres of fibroid necrosis surrounded by either lymphocytic infiltration or catarrhal oedema were seen, and calcium concrements were frequently found. In 8 cases marked oedema with diffuse regressive changes of the ganglionic cells was established. In 5 of the cases perivascular lymphocytic infiltration was observed, most prevalently in the diencephalon and mesencephalon.

The author concludes that the central nervous system is involved very frequently in rheumatic infections, but since cerebral rheumatism is seldom lethal, this contention is difficult to prove. Two changes are possible in the brain—diffuse (serous exudation and changes in the protoplasm) or proliferative, with infiltration. Diffuse changes are much the more dangerous, since they affect a larger part of the brain and damage the protoplasm of the ganglionic cells. Fibroid necrosis in the choroid plexus is characteristic of the rheumatic process. It is suggested that the brain becomes involved when the rheumatic agent enters the cerebrospinal fluid (C.S.F.). Under the influence of gravity, the pathologically changed fluid accumulates in the lowest parts of the fluid system, that is, at the bottom of the third ventricle, and in the basal cisterns. Hence the diencephalon with its important vegetative centres is affected. Once the rheumatic agent has entered the C.S.F. there are no more obstacles to its advance, since it is re-absorbed by the ependyma. This explains the presence of acute and chronic changes in the hypothalamic centres. It is considered possible that inflammation of spinal roots is also caused by rheumatism.

Dushanka Wolstenholme

1381. **Phenylcinchoninic Acid Derivatives (HPC) in Rheumatic Fever and Diabetes Insipidus.** (Fenylcinkoninbehandling (HPC) av diabetes insipidus och akut artrit)

S. HELANDER. *Nordisk Medicin* [*Nord. Med.*] **47**, 10–13, Jan. 4, 1952. 4 figs., 9 refs.

The author reports the results of treatment of 3 cases of diabetes insipidus, 5 of rheumatic fever, and 5 of rheumatoid arthritis with hydroxyphenylcinchoninic acid (HPC) and 3-hydroxy-2-phenylquinoline-4 : 8-dicarboxylic acid in the Karolinska Hospital, Stockholm. In diabetes insipidus the antidiuretic effect of HPC, given by mouth in 3 doses of 25 mg. daily, was striking, the volume of urine being immediately reduced to one-third of its previous value. It was found in one case that an identical antidiuretic effect was obtained with a much smaller dose of the dicarboxylic acid derivative (75 mg. daily). However, with both drugs diuresis recurred when treatment was stopped. These preparations had no effect on normal water diuresis.

In 3 of 5 patients suffering from typical acute rheumatism, treatment with HPC caused a fall in temperature and disappearance of swelling and pains within 24 to 48 hours; one case was complicated by bronchopneumonia, which necessitated penicillin treatment and prevented temperature from returning to normal for several days, while the fifth patient required larger doses before joint pains and temperature were significantly improved. Comparison between HPC and the dicarboxylic acid derivative showed that although these two compounds had a similar antidiuretic effect, the dicarboxylic acid derivative was less effective as an antipyretic. In one patient suffering from an accompanying carditis, a second-degree heart block developed which, however, disappeared in 4 days. In 5 cases of rheumatoid arthritis, no objective improvement occurred with HPC, although the patients stated that the pain and stiffness in the joints was reduced. Of 21 patients treated for various disorders with these compounds only 2 complained of nausea and one developed urticaria.

The author, in contrast to Marshal and Blanchard, who first reported the specific action of these drugs (*J. Pharmacol.*, 1949, **95**, 185), suggests that their point of attack is in the cells of hypothalamus, where the body-temperature-regulating centre and the cells regulating the secretory activity of the posterior pituitary lie in close proximity. He points out that the previously known antipyretic, antirheumatic, and analgesic drugs, like the phenylcinchoninic acid derivatives, have the same effects in varying degrees and suggests that their mode of action is essentially the same. The increased excretion of uric acid produced by these drugs has been attributed to their action on the anterior lobe of the pituitary, partly because this effect is absent when the pituitary is removed, and partly because ACTH has a similar action. If this proves to be correct, it may be assumed that the antirheumatic effect of these preparations also is due to their action on the anterior pituitary. However, since their effect on rheumatoid arthritis, for example, is not comparable with that of ACTH, the author believes that these preparations act primarily on the hypothalamus, through which they stimulate the production of anterior-lobe hormone. *E. S. Fountain*

1382. **Intravenous Therapy in Acute Rheumatic Carditis.** (Les perfusions veineuses dans le traitement de la maladie de Bouillaud)

J. OLMER, E. GASCARD, and G. BOUSQUET. *Annales de Médecine* [*Ann. Méd.*] **52**, 197–224, 1951. 10 figs., 11 refs.

The authors give a detailed account of 11 cases of acute rheumatic carditis treated by slow intravenous therapy with sodium salicylate (3 to 12 g. daily) or sodium gentisate (6 g. daily), with or without heparin, for periods of 3 to 9 days. The patients were young adults, acutely ill, some having had previous attacks of rheumatic fever. In most of the cases previous oral therapy with antipyrine or salicylates had given little or no relief.

Only 1 case showed dramatic response to the intravenous therapy; 8 others showed some improvement in the general condition but without any alteration in the heart condition. In 2 cases intravenous therapy had no effect whatever. It is concluded that intravenous therapy is not advantageous in the treatment of acute rheumatic carditis, and where salicylates have proved ineffective the

authors prefer to use such other remedies as antipyrine, antibiotics, chrysotherapy, or (in articular rheumatism) ACTH or cortisone. They emphasize once again the absolute necessity for prolonged rest.

Kathleen M. Lawther

CHRONIC RHEUMATISM

1383. **The Speranskii Method of Spinal Pumping in the Treatment of Arthritis**
J. H. Robbins and P. H. Settlage. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **222**, 663–676, Dec., 1951. 1 fig., 15 refs.

A review of previous reports on the Speranskii spinal pumping treatment of arthritis is given and the results in a new series of cases treated in the Madison General Hospital, Wisconsin, are described. The technique used was slowly to withdraw and reinject 10 ml. of cerebrospinal fluid 20 times, each phase taking at least 45 seconds. Finally 10 ml. was withdrawn.

Only 6 of 26 cases of rheumatoid arthritis and one of 5 cases of ankylosing spondylitis showed major improvement. The results in osteoarthritis were better, marked improvement occurring in 7 out of 11 cases. Erythrocyte sedimentation rate was unaffected. There were no protracted ill effects from the treatment, though nausea and headache lasting up to 10 days occurred in 18 cases. Improvement could not be correlated with such reactions. Details of 4 cases in which dramatic improvement occurred are given.

The authors are [rightly, the abstracter considers] cautious in their conclusions, but feel that the treatment warrants further trial. In a final note a death from cerebellar pressure cone following Speranskii pumping is recorded. A malformation is presumed, but not proved.

H. F. Turney

1384. **Cortisone and A.C.T.H. in Treatment of Ankylosing Spondylitis**
F. D. Hart. *British Medical Journal* [*Brit. med. J.*] **1**, 188–190, Jan. 26, 1952. 4 refs.

In view of the confusion caused by the American practice of including cases of ankylosing spondylitis in series of cases of rheumatoid arthritis subjected to clinical trials, the author studied the effect of treatment with ACTH (corticotrophin) on 6 selected cases of ankylosing spondylitis at the Westminster Hospital in order that the effect of the hormone on this disease entity could be estimated more clearly. He found that the early acute cases benefited most, although dosage was low and periods of administration were short. One case, which was of long standing, showed no improvement. In one case, treated during an acute episode, no rebound occurred after gradual withdrawal of the drug, and remission has now persisted for a period of 8 months.

The conclusion drawn by the author is that since ACTH is scarce its employment might reasonably be restricted in this disease to periods of painful exacerbation, to allow other, more slowly effective, methods of therapy to be instituted. He feels that the classical basic treatment of this disease remains unchanged by the advent of adrenal hormone therapy, although a potent short-term weapon is now available for use during the more acute episodes.

W. S. C. Copeman

1385. **Generalized Osteoarthritis and Heberden's Nodes**
J. H. Kellgren and R. Moore. *British Medical Journal* [*Brit. med. J.*] **1**, 181–187, Jan. 26, 1952. 9 figs., 16 refs.

From a study of 391 cases of osteoarthritis the authors have defined a clinical entity which they term primary generalized osteoarthritis. This entity occurs most frequently in middle-aged women, and is characterized by a distinct pattern of joint involvement which they describe in detail. Each affected joint passes through an initial painful and more or less acute arthritic phase, and since this process is not confined to the terminal phalanges of the fingers (where it is well recognized) there is a danger of the condition being mistakenly diagnosed as rheumatoid arthritis. The other clinical and radiological features which distinguish this syndrome are well described.

The authors regard generalized osteoarthritis as a constitutional disease resulting from an inherited defect similar to that which gives rise to "idiopathic" Heberden's nodes. They consider that much can be done to help sufferers from this disease by the proper management of their complaints, although there is no specific treatment available.

W. S. C. Copeman

1386. **Ultrasonic Wave Therapy in Osteoarthritis of the Hip Joint**
T. de Preux. *British Journal of Physical Medicine* [*Brit. J. phys. Med.*] **15**, 14–19, Jan., 1952. Bibliography.

The author reports his experience in the treatment of osteoarthritis of the hip-joint with ultrasonic waves. He is inclined to compromise between the excessive optimism of some and the negative attitude of others in assessing the usefulness of this form of therapy in osteoarthritis. The technique is useless in rheumatoid arthritis and of limited value in ankylosing spondylitis, in which condition deep *x*-ray therapy remains the treatment of choice.

In analysing the results of treatment he divides his 200 cases into three grades according to the extent of the radiological changes in the joint: (1) Of early cases about one-third failed to respond; in another third marked lessening of pain and stiffness and increase in movement were observed, and in the remainder only partial improvement with a dulling of pain was obtained. (2) In moderate cases nocturnal pain was usually suppressed after 8 to 10 treatments. Pain on weight-bearing was usually more difficult to control. One advantage of ultrasonic over deep *x*-ray therapy is that treatment can be repeated as often as is necessary. There can be no standard technique for all cases; some may need as many as 30 treatments to be fully effective. Favourable changes in *x*-ray appearances were observed in this group, such as disappearance of pseudo-cysts and healing of articular erosions, but the author admits that without examination of a control series these changes

might well be regarded as fortuitous. (3) In cases in which there are gross bony changes and dislocation, ultrasonic therapy was found to be of value only if the case was not suitable for surgery and had failed to respond to other forms of conservative treatment.

The generator used by the author is of the Siemens type (" sonastat ") with a frequency of 800 kilocycles, a quartz surface of 10 sq. cm., and a maximum output of 50 watts (5 watts per sq. cm.). The treatment is given through three fields (anterior, lateral, and posterior) and the average intensity used for treatment of the hip-joint is 15 to 20 watts per sq. cm. Pain is avoided by using as low an effective intensity as possible. The total time for each treatment is about 30 minutes, treatment being given twice weekly. In advanced cases 15 to 30 treatments are given. In successful cases treatment is repeated at yearly intervals starting 6 months after the first treatment, which is reported to keep symptoms in check. The author concludes that, compared with other types of conservative treatment, ultrasonic therapy is one of the best methods available to-day for the treatment of osteoarthritis of the hip. *M. H. L. Desmarais*

RHEUMATOID ARTHRITIS

1387. **Problems of Prolonged Cortisone Treatment for Rheumatoid Arthritis. Further Investigations**
R. H. Freyberg, C. H. Traeger, M. Patterson, W. Squires, C. H. Adams, and C. Stevenson. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 1538–1543, Dec. 15, 1951. 3 figs.

From the Hospital for Special Surgery and Cornell University Medical College, New York, the authors give an account of the results of cortisone therapy in 44 patients (25 women and 19 men) suffering from rheumatoid arthritis. The patients received cortisone for periods ranging from 100 to 400 days. No attempt was made to produce a complete remission, because of the high dosage that would be required and the frequency of undesirable side-effects that this would entail. By using no more than 75 mg. of cortisone daily, complications were readily corrected or controlled. In a few patients as little as 25 mg. daily produced a satisfactory response, but usually 50 mg. or more daily was required. Complications were considerably more frequent in female patients. Diabetes and hypertension did not develop gradually during prolonged treatment; if these complications occurred they did so in the early weeks of treatment. Treatment was discontinued in 6 patients because of complications, which were as follows: diabetes, 1; mental depression, 1; oedema and poor benefit, 2; massive gastro-intestinal haemorrhage, 2.

Cortisone was discontinued in 24 others for various reasons, and their withdrawal symptoms were studied. In only 4 patients was improvement maintained for longer than 60 days after cortisone was withdrawn. Relapse occurred as often in cases treated for long periods as in those treated for short periods. A severe " withdrawal syndrome " occurred in 4 women and 1 man. When cortisone treatment must be stopped, this should be done slowly, the authors consider, by gradual reduction of dosage.

They conclude that there is no evidence that the course of the arthritis is ultimately altered favourably by prolonged cortisone therapy as they used it. They do not consider that the administration of cortisone is practical as a routine treatment, nor that it is an adequate treatment in itself. They prefer to use it for a definite purpose, such as to check rapidly worsening disease or to facilitate physical therapy and rehabilitation. *C. E. Quin*

1388. **Hematologic Changes with ACTH and Cortisone Therapy of Rheumatoid Arthritis**
S. C. Finch, C. L. Crockett, J. F. Ross, and T. B. Bayles. *Blood* [*Blood*] **6**, 1034–1050, Nov., 1951. 7 figs., 29 refs.

The haematological changes induced by treatment with ACTH and cortisone were observed in 20 patients with rheumatoid arthritis and other collagen diseases. A significant reticulocytosis occurred in every patient, the average peak being on the 9th day with ACTH and the 13th day with cortisone, its magnitude being unrelated to the initial degree of anaemia. In anaemic subjects the haematocrit and haemoglobin levels and erythrocyte count rose towards normal, but there was no change in these values in non-anaemic subjects or in those failing to show a clinical response to therapy. No patient became polycythaemic. Both hormones regularly caused a polymorphonuclear leucocytosis and eosinopenia, but lymphocytopenia was inconstant and not sustained. Apart from a reversion towards normal in the bone marrow of those patients who showed a moderate initial depression of erythropoiesis, there was no other change in the bone-marrow elements during or after therapy. Although the hormones had no effect on total blood volume, there was some degree of haemodilution during, and of haemoconcentration after, therapy, more marked with ACTH than with cortisone. Nevertheless, the most significant finding was a true average increase in erythrocyte mass of 18% at the end of treatment. This the authors believe to be a reflection of the control of the underlying disease rather than a primary effect on haematopoiesis. *Ellis Dresner*

1389. **Effect on Bleeding-time of an Extract of Blood of Patients with Rheumatoid Arthritis**
R. Greene, J. Vaughan-Morgan, and J. Gammon. *British Medical Journal* [*Brit. med. J.*] **1**, 17–21, Jan. 5, 1952. 2 figs., 11 refs.

Ungar, in work published in 1945 and subsequently, claims to have demonstrated in splenic extracts two pharmacologically opposed substances which he named " splenin A " and " splenin B ". The former is probably a derivative of ascorbic acid and the latter an ester of fatty acids with a complex alcohol. He later succeeded in demonstrating splenin B in human serum in various pathological conditions, including rheumatoid arthritis. Greene also found splenin B in the serum of patients with rheumatoid arthritis, but never in healthy persons, whose serum contained only splenin A. After successful treatment with ACTH, serum from rheumatic patients

contained splenin A but no splenin B. Ungar believes that both substances are produced in the spleen, and that their production forms part of the general adaptation syndrome.

In the present work, the authors set out to investigate the effects of sera from normal subjects and from patients with rheumatoid arthritis on the bleeding-time of guinea-pigs. Pooled, freeze-dried sera were used from which chloroform-soluble and acetone-soluble extracts were made. The former is said to contain splenin A and the latter splenin B. In a series of carefully controlled experiments, it was shown that the chloroform extract from normal serum decreases the bleeding time, and acetone extract from rheumatoid serum increases it. The results are statistically valid, and are shown in detail in tables. The authors conclude that a factor or factors present in the splenin A extract of normal serum reduces bleeding time, but is absent from similar serum extracts in rheumatoid arthritis. A factor or factors is present in the splenin B serum extract in rheumatoid arthritis that increases bleeding time, but is absent from normal serum. They add that their experiments give no indication of the manner or place of production of these substances. *Ellis Dresner*

1390. **Further Observations on the Use of Pregnenolone in Rheumatoid Arthritis**

G. N. Myers and D. N. Ross. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **10**, 432–440, Dec., 1951. 2 figs., 3 refs.

Four female patients suffering from rheumatoid arthritis were given a daily dose of 300 mg. pregnenolone by the intramuscular and sublingual routes for a period of 34 days. Two cases showed no improvement whatsoever; one showed a very minor clinical improvement; the fourth showed a more marked clinical improvement. Pregnenolone did not influence the serum content of sodium, potassium, or chlorides, nor had it any effect upon the creatinine/uric acid ratio. The leucocyte response to pregnenolone was not consistent. The two cases which showed no clinical improvement showed a reduction in the circulating leucocytes; the reduction in the other two cases was so small as to be negligible. —[Authors' summary.]

1391. **The Short-term Effect of Pitressin in Rheumatoid Arthritis**

G. G. Haydu and B. W. Haydu. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **223**, 1–8, Jan., 1952. 43 refs.

In a previous paper the authors had suggested that a heightened adenosine-triphosphatase (ATP) activity was an underlying factor in rheumatoid arthritis. It was subsequently reported that "pitressin" reduced this activity. It was therefore deduced that pitressin should alleviate the symptoms of rheumatoid arthritis.

To test this theory, 4 units of pitressin were given to 8 patients with osteoarthritis and trauma, and to 8 patients with rheumatoid arthritis; in the latter marked improvement of symptoms occurred in the majority within half an hour, although the improvement was evanescent. In the osteoarthritic and traumatic cases pitressin had no effect. Any possible ACTH-like action was ruled out, as an increase in the eosinophil count was found to occur. So far as they go the results support the original theory. It is emphasized that pitressin was used for research purposes and not as a form of therapy. *H. F. Turney*

1392. **Effect of Still's Disease on the Haemopoietic System**

B. Schlesinger and I. A. B. Cathie. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **10**, 412–417, Dec., 1951. 2 figs., 17 refs.

The authors point out that Still's disease may attack children suddenly without arthritis, and the diagnosis may be difficult in the early stages. The child may have fever and a rash, but the blood picture is the most characteristic feature of the disease at the early stage. There is a marked neutrophil leucocytosis up to 30,000 cells per c.mm. The leucocytosis then disappears and does not recur except in acute relapse. In spite of this blood picture it has never been possible to demonstrate any local or general infection, and antibiotics prove ineffectual in treatment. When the arthritic phase of the disease is established, the blood picture may show only some anaemia and relative lymphocytosis. In rare cases where the disease is particularly severe and malignant there may be a serious leucopenia.

Examination of the bone marrow made by the authors in 32 cases of acute Still's disease showed a granulocytosis and hyperplasia, and this appearance did not change when the peripheral blood no longer showed the leucocytosis. They suggest that there may be some inhibiting factor preventing the cells formed in the marrow from escaping into the blood stream. Experiments have shown that when the adrenal glands are stimulated by ACTH there is an increase in circulating neutrophil leucocytes; but the leucocytosis of early Still's disease is far greater than any evoked by ACTH. The authors raise the question whether this leucocytosis could be due to a "desperate stimulation of a damaged organ prior to exhaustion". Similarly they ask if there could be any relationship between Still's disease and leukaemia, but point out that there is so far no proof that leukaemia can develop in Still's disease. *W. Tegner*

1393. **Arthritis Mutilans.** [In Danish]

S. Rosendahl-Jensen. *Nordisk Medicin* [*Nord. Med.*] **45**, 923–925, June 13, 1951. 8 figs., 9 refs.

Arthritis mutilans is a rare disease of which only a few cases have been published. It affects mainly the hands and feet, although any joint may be affected. The joint surfaces are destroyed and there is concentric atrophy and destruction of the diaphysis. The destruction is most frequently seen in rheumatoid arthritis, but similar destruction is found in psoriasis and leprosy. Of 20 skeletons found in an old leper cemetery in Denmark 10 showed evidence of arthritis mutilans. Three new cases, all in patients with rheumatoid arthritis, are reported. *J. Agerholm*

Disorders of the Nervous System

1394. **Direct Measurement of Intravascular Pressure in Components of the Circle of Willis**
B. M. Bloor, G. L. Odom, and B. Woodhall. *Archives of Surgery* [*Arch. Surg., Chicago*] **63**, 821–823, Dec., 1951. 3 refs.

In 4 patients—one with an aneurysm and 3 with arterio-venous anomalies—measurements were made of the blood pressure within the intracranial part of the carotid and the middle cerebral arteries and the vessels concerned in the aneurysm. The apparatus used was an electromanometer attached to a fine needle placed in the artery. No ill effects ensued, though the aneurysm began to bleed when exposed, so that the right anterior cerebral artery had to be clipped. Individual variations in pressure were noted in the various patients, but there appeared to be a constant fall in arterial pressure along "the entire vascular segment" after occlusion.

[The authors' technique is open to the objection—as are all pressure recordings by needling arteries—that the neuromuscular mechanism of the vessel itself is disturbed and vascular reflexes are excited which may alter the state of the associated vessels.] *Lambert Rogers*

1395. **Nocturnal Epilepsy.** (L'épilepsie morphéique)
P. Passouant, H. Latour, and J. Cadilhac. *Annales Médico-Psychologiques* [*Ann. méd.-psychol.*] **109**, 526–540, Dec., 1951. 5 figs., 4 refs.

In a series of 50 epileptics whose attacks occurred entirely or chiefly at night, the clinical features observed were divided into those regarded as essentially epileptic and those regarded as "para-epileptic". Of the epileptic features, grand mal was seen in 38 cases; it was often preceded by clonic movements, sufficient in 2 cases to awaken the patient, and was usually the only attack that night, unless status epilepticus supervened (2 cases). Bravais–Jacksonian attacks were observed in 5 out of the 50. The "para-epileptic" features included somnambulism, paroxysmal pain (in the head in 2 cases and in the abdomen in one), insomnia, nightmares, dreams (up to 10 in one night in one patient who also had visceral and vasomotor equivalents), and hypnagogic hallucinations.

The attacks occurred during sleep in 38 cases, in the awakening period in 9, and while falling asleep in 3 of the 50 cases. Clinical features seen during the day included petit mal, automatism (in one case premonitory to a narcoleptic attack), and certain psychological disorders such as bouts of cyclothymia and, in 2 cases, suicidal tendencies. Electroencephalographic features included those characteristic of sleep, but recorded when the patient was awake. They consisted mostly of multiple rhythms made up of theta rhythm (4 to 7 c.p.s.) and a rapid rhythm of 15 to 22 c.p.s. These two types often showed periodicity, especially in frontal tracings; at other times only one was found as an isolated phenomenon. Sometimes the rapid rhythm was associated with a delta rhythm. The more specific characteristics included spikes and spiked waves occurring singly or in paroxysms. In general, the electroencephalogram suggested a deep origin for the epilepsy. In 30 cases a temporal basis was demonstrable, more frequently bilateral. In treatment the barbiturates were of little value, whereas cerebral stimulants, in small doses, sometimes produced excellent results. Hydantoinates may give some degree of improvement, but the best results were uniformly obtained with phenacetylurea.
I. H. Milner

1396. **The Effect of BAL (2:3-Dimercaptopropanol) on Hepatolenticular Degeneration (Wilson's Disease)**
D. Denny-Brown and H. Porter. *New England Journal of Medicine* [*New Engl. J. Med.*] **245**, 917–925, Dec. 13, 1951. 2 figs., 37 refs.

In hepato-lenticular degeneration it has been shown that there is a greatly increased copper content both of the liver and of the basal ganglia, and that the urinary output of copper is high. Administration of BAL causes a great increase in copper excretion (up to seven times the resting amount). A persistent amino-aciduria is also found in this disease, but this is unaltered by BAL.

The observation that after giving BAL there was an improvement in the clinical state of the patient has led the authors to treat 5 cases in this way at the Boston City Hospital, and they now record their results. Full clinical details of the patients are given; their ages ranged from 21 to 47 years, and they were all of the more chronic "pseudosclerotic" type. Results of the copper metabolism and other tests are also given.

Doses up to 7 mg. of BAL per kg. body weight were used, but these caused toxic reactions. No severe effects were found with 2·5 mg. per kg., though this dose was reduced in some cases because of vomiting. Injections were given twice daily for 10 to 12 days; the need to ensure that they are deeply intramuscular and not near nerves is emphasized.

Improvement usually began 14 days after completion of the course of treatment and continued for 2 to 3 months, but the patient's condition began to relapse within 3 to 6 months, improving again with another course of treatment. The authors consider that maintenance treatment will be required. The recommended routine is 1·0 to 1·5 ml. of BAL in peanut oil twice a day for 10 days every month until maximum improvement is obtained, and thereafter every second month.

The degree of improvement, the progress of which is described fully in the case reports, is remarkable, patients unable to move without assistance becoming able to look after themselves. It is of interest that after treatment in 2 cases the Kayser–Fleischer rings lost much of their brownish coloration, becoming more grey.
N. S. Alcock

Psychological Medicine

1397. **Psychiatric Aspects of Somatic Immunity. Differential Incidence of Physical Disease in the Histories of Psychiatric Patients**
J. W. L. DOUST. *British Journal of Social Medicine* [*Brit. J. soc. Med.*] **6**, 49–67, Jan., 1952. 32 refs.

The physical illness history, in terms of 38 bodily complaints and 72 somatic diseases, was assessed in 354 healthy adult controls and in 272 patients with a variety of psychiatric disorders. It was found that the physical illness experience of the psychiatric patients was significantly in excess of that of the controls, psychotics having a heavier loading of previous physical illness than neurotics or psychopaths. The influence of age and sex was insignificant in comparison with that of psychiatric diagnosis.

The childhood illness experience in all groups did not differ significantly with respect to most zymotic diseases. A differential pattern of organ system reaction was found to be present for other disorders. The somatic illness history of neurotics included many examples of minor physical disability, that of depressives showing especially a loading with gastro-intestinal disorders, and that of schizophrenics a loading with locomotor and cardiovascular diseases.

The findings are discussed with reference to their reliability and validity, and their immunological implications considered from the psychiatric point of view.—[Author's summary.]

1398. **Psychopathology of Cushing's Syndrome and Addison's Disease. Conclusions from a Comparison.** (Psychopathologie des Cushing-Syndroms und der Addisonschen Krankheit. Hinweise aus einem Vergleich)
M. BLEULER. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **81**, 512–513, June 2, 1951. 17 refs.

From the endocrinological point of view the syndrome of Cushing appears to be the exact opposite of Addison's disease—that is, a state of hyperfunction as opposed to hypofunction. This opposition in the field of the pathology of metabolism does not by any means find its counterpart in a corresponding psychopathological opposition. The psychopathological features of the two diseases are fundamentally and in their chief manifestations the same, consisting of relatively slight personality changes of the type of the brain-stem psychosyndrome, which may, in severe cases, be accompanied by acute exogenous reactions. In both types of disease there are alterations in disposition and humour, with depression or irritability, apathy or excitement, and dedifferentiation of the emotional life. The fundamental similarity in the psychopathology of the two syndromes is accounted for by the greater degree of differentiation in psychical than in bodily repercussions. The practical conclusion is as follows: "The clinical study and use of hormonal factors must not be seen detached from the personality but only in conjunction with the study and treatment of the individual personality".

G. Pflugfelder (*Excerpta Medica*)

1399. **The Importance of Hyperventilation in Differential Diagnosis**
W. I. TUCKER and J. M. ELLIOTT. *Lahey Clinic Bulletin* [*Lahey Clin. Bull.*] **7**, 185–191, Oct., 1951. 7 refs.

The frequency with which hyperventilation occurs is not generally appreciated; it was an important factor in 60 of 100 consecutive cases of anxiety neurosis or hysteria seen at the Lahey Clinic, Boston, Massachusetts. The symptoms may be related to the peripheral nerves (numbness, tingling, pain, and stiffness of extremities and face), to the central nervous system (faintness, giddiness, changes in consciousness), to the accompanying anxiety (sweating, tremulousness), to the cardiovascular system (palpitation, chest pain), or to the gastrointestinal system (dry mouth, belching, dysphagia). Details are given of 5 cases in which hyperventilation simulated epilepsy, cerebral tumour, phaeochromocytoma, hypoglycaemia, and gastro-intestinal disorder respectively.

H. McC. Giles

1400. **Morning Sickness in Men: a Functional Gastrointestinal Syndrome**
I. A. WARREN. *Gastroenterology* [*Gastroenterology*] **19**, 820–828, Dec., 1951. 5 refs.

In this study 20 male veterans were examined in a medical clinic of the U.S. Veterans Administration, whose main complaint was "morning sickness": the patient lacked appetite for breakfast; the sight of food in the morning, especially fatty food, was distasteful; and if he forced himself to eat there were nausea, retching, and perhaps vomiting. A small midday meal was eaten without enjoyment. By evening he could take a substantial meal and felt better. Nausea and sometimes vomiting often followed heavy manual work. The patients complained also of chronic fatigue. Many experienced abdominal pain and discomfort; bouts of diarrhoea with cramp-like pain were reported by half the patients. No organic disease could be found in 17; a duodenal ulcer was present in one, and a deformed duodenal bulb without ulcer crater in 2 others. In none of the series could gastric retention be demonstrated.

A diagnosis of psychoneurosis was made in every case. The precipitating factor of the illness was, in general, a situation which was disturbing to the patient. The author concludes that the syndrome reflects an attitude of distaste and rejection of the events of the coming day. Inability to "stomach" the approaching reality is manifested by the primitive rejection pattern of nausea and vomiting.

[The illustrative case records in this paper do not give the time of onset of the illness, or its setting, and there is no indication of the emotional state associated with vomiting. The author does not state how many of his patients were habitual drinkers.] *Desmond O'Neill*

1401. **Traumatic War Neuroses Five Years Later**
S. FUTTERMAN and E. PUMPIAN-MINDLIN. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **108**, 401–408, Dec., 1951. 8 refs.

The authors found that frequently traumatic war neuroses occur in non-combatant personnel in a dangerous area, and suggest that this frequency is due to the inability to give vent to effective motor discharge of the emotions. Guilt over attacking the defenceless is an important factor in the precipitation of illness. Neurosis occurs in conjunction with physical injury, especially if this leads to enforced immobilization. Speech disturbances may occur without previous trouble of a similar type. The patient tends to minimize any antecedent difficulties in order to accentuate the symptoms and their connexion with the traumatic experiences. He reacts to civilian life as if still in danger; but changes in the repetition of traumatic experiences are likely to indicate where these experiences are linked with pre-traumatic events.

The authors found that intravenous narcosis and hypnosis are not of great value in treatment. In the outgoing, or alloplastic, type of patient therapy is short and consists in relating past experiences to present feelings and attitudes; in the inhibited, or autoplastic, type the experiences can, in addition, be related to the pre-traumatic events. *G. de M. Rudolf*

1402. **Follow-up Study of Psychoneuroses. Preliminary Report**
N. Q. BRILL and G. W. BEEBE. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **108**, 417–425, Dec., 1951.

A series of 955 cases from all parts of the United States were investigated 5 years after the loss of at least one day of military or naval duty owing to psychoneurosis. Of these patients 592 were examined by psychiatrists, and information of the condition of 363 was obtained from written records.

Of the total number, 48% of those treated for psychoneurotic disorders in the Service had no appreciable emotional difficulty before enlistment, 14·6% had overt neuroses, and 20% had manifest personality disorders. Only 11% had shown moderately impaired, and 1·3% markedly impaired, function before enlistment. The factors precipitating breakdown were: combat in 42%; climate, physical demands, injury, illness, or prolonged overseas service in 14%; military frustrations in 12%; normal military stresses in 7·6%; economic hardship and domestic difficulty in 6·4%; and in 4·6% no stress was evident. Of the total 35% broke down before going overseas; 52% while overseas; and 13%, of whom 66% had been in combat overseas, after returning home. Discharge without return to duty took place in 39%, and after being returned to duty in 18%. The percentage returned to duty and never discharged on psychiatric grounds was 40%. On leaving the Service, 55% suffered from mild neurosis, 20% from severe neurosis, and 6% showed personalities associated with behaviour disorders. No disability was found at follow-up in 45%; disability was slight in 26·6%, moderate in 20·4%, severe in 7·5%, and total in 0·6%. Only 15% were unemployed, half because of illness. Improvement since returning to civil life occurred in 54%, and deterioration in 13%. The prognosis was good in 32% and poor in 17·4%; it could be improved by treatment in 31%.

Slight disability symptoms were present in 92% of those who were well integrated before enlisting, in 61% of the overt neurotics, and in 49% of those with pathological personalities. Of those severely or totally disabled, 66% were suffering from symptoms that were present before service. Of the slightly disabled group about 50% had symptoms present in civil life.

Of those with at least one parent with psychosis or neurosis and the other parent with emotional or personality disorder, 61% were at least moderately disabled. Parental withdrawal through death, divorce, or chronic illness before the age of 16 was entirely unrelated to degree of disability at follow-up. Combat and non-combat cases showed similar proportions of disability, but during service the combat cases deteriorated more than the non-combat cases. Severity and duration of combat were not related to disability, but of patients in combat at sea at least 43% were moderately disabled, in contrast to 27% of those in combat on land.

Of those whose illness was severe 39% were at least moderately disabled, whereas the figure for slight illness was only 20%. Of those discharged when well 91% were not disabled, but of those discharged when suffering from severe neurosis only 21% were well at follow-up. Since discharge 60% of those who were now severely or totally disabled became worse, but 69% of those without disability at follow-up improved. With regard to occupation, 92% of the severely disabled were maladjusted.

Of those with overt neurosis before entering the Service, 30% were demobilized without medical discharge, 32% served overseas, and in 18% breakdown occurred only under stress of combat. About 60% of those discharged for disability were capable of working full time when discharged. In only 19% was it believed that compensation had a harmful effect. The results suggested that discharge for disability may contribute to perpetuation or aggravation of neurosis. *G. de M. Rudolf*

1403. **Glutamic Acid and Mental Deficiency**
K. ALBERT, P. HOCH, and H. WAELSCH. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **114**, 471–491, Dec., 1951. 1 fig., 8 refs.

At the New York State Psychiatric Institute L-glutamic acid was given to mentally retarded children (excluding those with a history of convulsive disorders) for a period of 4 months in a daily dosage of 10 to 12 g. divided into 3 doses, one before each meal. This was preceded or followed in some cases by a similar period in which lactose tablets were given, while in others a second period

of glutamic acid treatment was given. A control group were given lactose during both periods. During each treatment period, and before and after the experimental period as a whole, assessment by means of a variety of psychological tests was carried out, the psychologist applying the tests being unaware whether the patient was receiving glutamic acid or the placebo.

The Bender visual motor gestalt designs test was applied to 34 individuals, and 2 psychologists independently picked out the best from among all the drawings by each patient; in 30 and 27 cases respectively these proved to be from the test carried out during glutamic acid medication. With Form M of the revised Stanford–Binet test in cases in which the initial I.Q. was low (34 to 53), an increase occurred in 17 of 27 defectives following the administration of lactose, and in 18 of 25 following treatment with glutamic acid. An increase occurred in all of 9 patients, with an initial I.Q. of 34 to 44, who were given 2 periods of glutamic acid treatment. An increase in I.Q. also took place in all of 16 patients who were given glutamic acid first, a fall occurring after the subsequent period of lactose administration in 11 of these. All of 8 patients with a higher initial I.Q. (54 to 67) showed a rise in I.Q. after glutamic acid, but out of 5 others who were given lactose only, 4 showed a similar rise.

In the low-I.Q. group, the parents reported an increase in motor activity, aggressiveness, work, appetite, and talking about twice as frequently in the glutamic acid periods as in the lactose periods. In the higher-I.Q. group, interest, energy, sociability, speech, speed, self-confidence tended to increase more in the glutamic acid periods than in the lactose periods. The increases in I.Q. were statistically significant and appeared in all types of sub-test of Form M. The extent of the increase was, however, small, rarely being sufficient to be of practical or clinical importance; it varied from 1 to 3 points after administration of lactose and from 1 to 25 points after glutamic acid. In 20 of 22 cases in which Form M was applied again some months after the cessation of glutamic acid treatment the I.Q. had fallen 1 to 9 points, and in all of 8 cases in which lactose had been given it had fallen 1 to 5 points.

[These authors did not follow Zimmerman's method of raising the dose until over-activity occurs, and then slightly reducing it.] *G. de M. Rudolf*

1404. **Sympathetic Blockade in the Treatment of Anxiety States**

S. SMITH. *Journal of Mental Science* [*J. ment. Sci.*] **98**, 161–166, Jan., 1952. 8 refs.

Cases of anxiety neurosis were treated with hexamethonium bromide, with the object of relieving severe somatic manifestations which had made psychotherapy difficult; 12 female and 5 male patients were treated, and the symptoms particularly considered were tension, sweating, palpitations, and tremor. All the patients had received psychotherapy and sedation for from 1 to 9 months before the experiment, and 3 had had electroplexy.

Most of the subjects were treated as out-patients. Hexamethonium bromide was given orally in doses of 0·25 g. twice daily after meals for 5 days. The dose was increased by 0·25 g. daily every 5 days to a maximum of 1·25 g. daily. Positive results obtained were maximal between the 6th and 10th weeks of treatment. [It is not stated for how long this was continued.] Renal disease and cerebral or coronary vascular incidents were considered contraindications. Toxic symptoms comprised nausea during the 2nd week in half the patients, transient anorexia in 3, and transient blurring of vision in one.

The tabulated results show that tremor was greatly relieved in 7, relieved in 9, and not relieved in one patient. Sweating was greatly relieved in 4, relieved in 11, and not relieved in 2. Palpitations were relieved in 13, and not relieved in 4. Tension was greatly relieved in one case, relieved in 12, and not relieved in 4. It would appear from this that objective manifestations respond somewhat better than subjective symptoms. The results were least satisfactory in cases with a strong depressive element. The blood pressure was not very markedly lowered with the dosages employed. The author concludes that " hexamethonium is an effective adjuvant in the treatment of anxiety states ". *R. Emery*

1405. **A Theory of E.C.T. Action and its Bearing on the Biological Significance of Epilepsy**

M. ROTH. *Journal of Mental Science* [*J. ment. Sci.*] **98**, 44–59, Jan., 1952. 4 figs., bibliography.

The changes produced by electric convulsion therapy (E.C.T.) in the electroencephalographic (EEG) pattern are discussed. These are correlated with the known clinical and physiological effects, and a diencephalic origin is deduced for both. Latent EEG changes brought out by light thiopentone anaesthesia argue an origin from a midline structure linked symmetrically to both hemispheres. Physiological changes, such as alteration in sleep rhythm, appetite, and weight, suggest that E.C.T. acts on diencephalic centres. In view of the many diverse uses to which E.C.T. is put in the treatment of mental illness, it would seem that the effect may be in the nature of producing homoeostasis, being inimical to recently formed morbid behaviour patterns and tending to restore long-established ones. The higher-voltage, low-frequency EEG waves demonstrated under light thiopentone anaesthesia during and after E.C.T. represent the rhythmic discharge in unison of many neurone clusters, and it is this activity which disrupts the abnormal patterns.

The epileptic fit, induced as it is by a variety of noxious influences, may be of biological significance as a means by which the central nervous system re-establishes homoeostasis in conditions which threaten its integrity.

The results in 45 patients from whom serial EEG's were made under light thiopentone anaesthesia, before, during, and after E.C.T. are given and discussed.

R. Emery

1406. **Pulse-wave Electrocoma**

E. B. STRAUSS, J. GOULD, and A. MACPHAIL. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **15**, 59–63, Feb., 1952. 3 figs., 3 refs.

Infectious Diseases

1407. **Chloramphenicol (Chloromycetin) in the Treatment of Experimental Relapsing Fever**
R. B. HEISCH and A. E. C. HARVEY. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **46**, 65–70, Jan., 1952. 1 fig., 3 refs.

Patients with general paralysis, together with white rats and monkeys, were experimentally infected with *Spirochaeta duttoni*, the causative agent of East African relapsing fever. (All such tick-borne strains of spirochaete have in common a tendency to cause relapsing infections in human beings and residual brain infections in laboratory animals, whereas in the louse-borne disease relapses are less common.) When spirochaetes had been present in the blood for 1 or 2 days, chloramphenicol was given by mouth every 4 hours for 72 hours, the dosage for 2 human subjects being 150 mg. per kg. body weight daily, for 10 rats 500 mg. per kg., and for 7 monkeys 600 mg. per kg. The primary attack was shortened in all cases and neither of the human patients relapsed. In the animals, however, relapses, though delayed, were not prevented, although the incidence was lower than in the controls. Moreover, several of the treated rats developed residual infections of the central nervous system. *G. M. Findlay*

1408. **Some Clinical Observations on the Prophylactic and Therapeutic Use of Proguanil in Mackinnon Road**
R. M. JOHNSTONE. *Journal of the Royal Army Medical Corps* [*J. roy. Army med. Cps*] **97**, 461–467, Dec., 1951. 6 refs.

The author reports the failure of proguanil to provide effective prophylaxis against *Plasmodium falciparum* infections in military personnel in East Africa. In a mean population of 1,200 ± 200 there were 122 cases of falciparum malaria in a year (1949–50), although all were supposed to be taking 100 mg. of proguanil daily. On investigation it was found that among the infected the prophylactic history was satisfactory in 74 cases, unsatisfactory in 27, and unknown in 21. Precipitating factors, including dysentery or diarrhoea, tonsillitis, and infective hepatitis, were established in a proportion of the cases. Among the 74 with a satisfactory prophylactic history, however, there were 28 cases in which there was no precipitating factor and no apparent reason for the development of malaria. The author found malarial parasites present in the blood of 25 patients admitted to hospital for other reasons and in whom there was no overt sign of malaria. He also quotes the results of an investigation in which 200 men took 100 mg. of proguanil daily under the supervision of an officer. The blood was examined before the start of the experiment and again on the 30th day. Parasites were found in one case before the experiment and in 5 on the 30th day. No attack of clinical malaria was observed among the subjects at risk during this time. Discussing the possible causes of failure, the author suggests that the drug may not be so effective against the pre-erythrocytic stage of the parasite as has been supposed. *William Hughes*

1409. **Effects of ACTH on Induced Malaria in Man**
E. H. KASS, Q. M. GEIMAN, and M. FINLAND. *New England Journal of Medicine* [*New Engl. J. Med.*] **245**, 1000–1002, Dec. 27, 1951. 3 figs., 14 refs.

The authors injected trophozoites of the McCoy strain of *Plasmodium vivax* intravenously into 10 middle-aged patients who were suffering from syphilis of the central nervous system; 3 were treated with ACTH (corticotrophin) by intramuscular injection in doses of 25 to 105 mg. 6-hourly, starting after the third paroxysm and continuing through the next 2 or 3, the patient being allowed to undergo 1 or 2 more paroxysms after stopping the ACTH before the infection was terminated with antimalarial drugs; the other 7 patients served as controls. Observations were made of the patients' temperature and of the numbers of parasites in the blood; it was found that the periodicity of the febrile attacks and the height of the fever were not affected by ACTH administration, but the treated patients showed more malarial parasites in the peripheral blood than the controls. Similar results were obtained in earlier experiments with *P. knowlesi* in monkeys and with *P. berghei* in rats. The authors suggest that the greater parasitaemia in the treated patients may have been due to a decrease in host resistance caused by ACTH. *J. F. Corson*

1410. **Treatment of Schistosomiasis**
B. GIRGIS and A. MAGID. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **46**, 81–84, Jan., 1952. 7 refs.

Sodium antimony tartrate given for the treatment of schistosomiasis in a total dose of 12 mg. per kg. body weight in 6 equal injections on 2 successive days causes, at any rate in Egypt, a considerable number of severe toxic reactions. A total dose of 15 mg. per kg. given over a period of 6 days to 28 patients caused much fewer reactions, and a cure rate of 67·8% was obtained, 25 of the patients being cured (3 of the patients thus treated had had previous relapses). It is considered that the optimal dosage of this drug is between 12 and 15 mg. per kg. body weight in a period of 6 days. *G. M. Findlay*

1411. ***Geotrichum* Septicemia**
R. A. BENDOVE and B. I. ASHE. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 107–110, Jan., 1952. 1 fig., 6 refs.

The genus *Geotrichum* contains several species which have been isolated from the stools or sputum of apparently normal persons. Occasionally bronchitis or lesions of the lung simulating tuberculosis have been

reported as being due to *Geotrichum* infection. In the case here described a species of *Geotrichum* was isolated from the blood. Administration of neomycin sulphate, 1,000 units per kg. body weight daily in 6-hourly doses, was continued for 3 days, after which the dose was halved for 9 days. The temperature fell gradually, and 8 days after beginning treatment the blood culture was still positive; after 15 days' treatment it was sterile. Impairment of hearing was noted on the 11th day of neomycin therapy and persisted up to the time of reporting, when the sputum still contained *Geotrichum* occasionally.

G. M. Findlay

1412. **The Liver in Sarcoidosis**

H. SHAY, J. E. BERK, M. SONES, E. E. AEGERTER, J. K. WESTON, and A. B. ADAMS. *Gastroenterology* [*Gastroenterology*] **19**, 441–459, Nov., 1951. 5 figs., bibliography.

At Temple University Hospital, Philadelphia, 24 patients diagnosed as suffering from sarcoidosis were examined by the authors. Needle biopsy of the liver was performed in 21 cases. Serial hepatic function tests were carried out, including the bromsulphalein retention test and a " liver profile " consisting of serum bilirubin and alkaline-phosphatase levels, cephalin–cholesterol flocculation, colloidal gold, thymol turbidity, and gamma-globulin flocculation tests, and estimation of serum lipoid content. Electrophoretic analysis of the serum proteins was carried out in 13 cases.

The results are discussed in detail and the conclusion is reached that the liver is commonly involved in sarcoidosis, both functionally and structurally. Focal granulomata were found in liver biopsy specimens in 16 of 21 patients. The lesions were sometimes isolated, sometimes diffuse; parenchymatous degeneration, lymphocytic and epithelioid infiltration, and sometimes giant cells were present in some; in others there was considerable fibroblastic activity. In the liver function tests deviations from normal occurred in active cases, especially in the flocculation tests, and notably in that for gamma globulin. Bromsulphalein retention was also observed in 14 of 23 patients. Increase in total serum protein content with a fall in albumin level and a rise in globulin level, especially that of gamma globulin, was common in the acute stages. Normal values were obtained in " healed " cases. The results of the zinc sulphate turbidity test were found to parallel closely the gamma-globulin level, and the authors suggest the former technique as a reliable method of following the course of the disease.

B. G. Maegraith

1413. **Boeck's Sarcoid with Involvement of the Central Nervous System**

W. H. PENNELL. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **66**, 728–737, Dec., 1951. 37 refs.

The author has found 51 cases of affection of the central nervous system in sarcoidosis reported in the literature, and he adds 3 others. He comments on the frequency of diabetes insipidus as a manifestation of the condition, as instanced by his first patient (aged 19), in whom diabetes insipidus was the cardinal symptom. Cervical adenopathy was present, and radiological examination of the chest showed a degree of infiltration. The tuberculin test gave a negative reaction. Injections of vasopressin decreased the polydipsia and polyuria [no figures are given]. The author assumes that the diabetes insipidus was caused by a sarcoid lesion of the pituitary gland.

He then draws attention to the occurrence of meningeal lesions in sarcoidosis, and describes 2 cases in which cerebrospinal-fluid analysis revealed a low sugar content —28 to 32 mg. per 100 ml. in one and 10 mg. per 100 ml. in the other. In the first case—in a negro aged 48—a coexisting skin lesion was biopsied and shown to be sarcoid. The Wassermann and tuberculin tests gave negative reactions. This patient had three episodes of headache together with neck stiffness associated with deafness and other cranial-nerve symptoms. He died 5 years after the onset of his first attack, but post-mortem examination was not carried out.

The second of these 2 patients was a negro woman of 25 who developed headaches in association with bilateral iridocyclitis. Bilateral pyramidal signs were elicited and a sensory level to D 2. Examination of the cerebrospinal fluid showed, in addition to the low sugar content mentioned above, a moderate pleocytosis ranging up to 94 cells per c.mm. (75 lymphocytes) and a protein content of 264 to 100 mg. per 100 ml. Section of a cervical lymph node revealed destruction of the architecture by a non-caseating granulomatous process. Wassermann and tuberculin reactions were negative. The patient was treated with cortisone without apparent improvement.

The author comments that the low sugar content of the cerebrospinal fluid in these cases gives added support to the theory that the agent responsible for sarcoidosis is infectious in nature.

Fergus R. Ferguson

VIRUS DISEASES

1414 (*a*). **Murray Valley Encephalitis: Isolation and Characterization of the Aetiological Agent**

E. L. FRENCH. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 100–103, Jan. 26, 1951. 8 refs.

1414 (*b*). **Murray Valley Encephalitis: Clinical Aspects**

E. G. ROBERTSON. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 103–107, Jan. 26, 1951.

1414 (*c*). **Murray Valley Encephalitis: Pathological Aspects**

E. G. ROBERTSON. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 107–110, Jan. 26, 1951. 10 figs., 5 refs.

1414 (*d*). **Murray Valley Encephalitis: Surveys of Human and Animal Sera**

S. G. ANDERSON. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 110–114, Jan. 26, 1951. 4 refs.

Murray Valley encephalitis is the name given to a virus disease which was first recognized in epidemic form in the Murray Valley in northern Victoria in the first 3 months of 1951. The present series of papers describes various aspects of the outbreak and of investigations which have been carried out into the disease.

In the first paper the author describes the isolation of the virus from the brain in 3 fatal cases. The technique of cultivating virus on the chorio-allantoic membrane of developing chick embryos is described in detail. From these infected membranes a complement-fixing antigen was prepared. The author concludes from the results so far obtained that the virus is serologically related to, though not identical with, that of Japanese encephalitis B, and a further study of its relationship to other encephalitis viruses is now in progress. Attempts to isolate the virus from blood, cerebrospinal fluid, and throat-washings were uniformly negative.

The author of the second paper discusses the clinical aspects and describes the course of the disease in detail as it occurred in 4 infants (2 of whom died), in 9 older children (of whom 2 died), and in 13 adults (of whom 4 died). The younger the patient, the more rapid was the course. The symptoms were generally those of any acute viral encephalitis. Recovery from the acute phase may leave gross cerebral injury, and several of the patients studied are merely vegetative survivors. There was, however, great variability in the symptomatology in the epidemic as a whole, many mild cases occurring without serious consequences in which the appearance of antibody in the blood clinched the diagnosis. A similar form of encephalitis was described in 1917 and 1918 under the name " Australian X disease ".

Discussing the pathological changes encountered in this disease, the author of the third paper in the series states that in the acute phase neurones were obviously attacked. Widespread necrosis was found, especially involving the cerebellum and thalamus, and in this respect the disease seems to differ from Australian X disease as examined by Cleland and Campbell in 1918. Secondary degeneration of nerve fibres sometimes occurred on an extensive scale. Reactive changes were less striking than might have been expected from those found in similar types of inflammatory encephalitis. Microglial response was an early phenomenon, and lymphocytic infiltration of moderate extent was also noted. At a later stage astrocytic proliferation was seen, and became more marked with time. The distribution of lesions was both diffuse and focal, chiefly in grey matter. Purkinje cells might disappear from the cerebellum in the acute phase with little evidence of inflammatory reaction. In the chronic stages total necrosis was especially noticeable in scattered foci in the basal ganglia and pons, while there were large areas of disintegration in the thalamus and diffuse or focal degenerative patches in all parts of the cerebellar cortex, calcium salts being deposited in these areas. (Photomicrographs illustrating these changes are reproduced.) All in all, it appears that the damage caused by this virus may be severe and widespread, but as with most diseases of the nervous system, for each " classical " example many mild, and still more subclinical, cases are to be expected.

This view is supported by the findings, reported in the final paper, in the examination of a large number of blood sera, both from healthy people and from clinical and suspected cases of the disease in various parts of Victoria, by means of the complement-fixing antigen mentioned above. Sera from various species of animal were also tested, many (such as the fox and opossum) giving positive results. The authors conclude from these tests that the 40 known cases of Murray Valley encephalitis which occurred in 1951 were probably all due to infection with a single strain of virus, which is widely distributed throughout eastern Australia, since complement-fixing antibody was detected in the blood of apparently healthy persons, and also in that of horses, over an area stretching from Cairns on the north-east coast of Queensland to the Great Dividing Range, which forms the southern boundary of the Murray Valley and appears to form a natural barrier to further spread of the disease, no case of infection with the virus being known to have occurred in southern Victoria. The occurrence of antibody in the blood of a variety of wild and domestic birds suggests that the epidemiology of Murray Valley encephalitis may resemble that of the Japanese and American types of virus encephalitis, birds acting as the primary reservoir from which the disease is transferred to man by mosquitoes. *Joseph Ellison*

1415. **Infectious Mononucleosis: the Prognostic Significance of Various Changes of the Blood Leukocytes**
J. E. STEVENS, E. D. BAYRD, and F. J. HECK. *Blood* [*Blood*] **7**, 31–36, Jan., 1952. 12 refs.

The authors studied at the Mayo Clinic 25 cases of infectious mononucleosis in which there were 50% or more lymphocytes in the peripheral blood smear. Differential counts of the lymphocytes were made according to Downie and McKinlay's classification. Type III lymphocytes were recognized in 16 cases, but were predominant in only one case. The authors could find no relation between the predominant type of lymphocyte and the severity of the disease. Granulocytic immaturity was present in 6 smears, of which 4 were from severe cases. Toxic changes in the leucocytes were also noted in severe cases. *Ernest T. Ruston*

See also Bacteriology, Abstract 1217.

1416. **An Outbreak of Epidemic Pleurodynia, with Special Reference to the Laboratory Diagnosis of Coxsackie Virus Infections**
A. S. LAZARUS, E. A. JOHNSTON, and J. E. GALBRAITH. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **42**, 20–26, Jan., 1952. 13 refs.

In September, 1950, an outbreak of pleurodynia occurred at Hoquiam, in the State of Washington. By the end of the month about 50 cases had been recorded, a known morbidity rate of about 5 per 1,000 of the population. The main symptoms were fever, abdominal pain, nausea and vomiting, headache, stiffness of the neck, and soreness of the throat, chest, and limbs. All patients recovered without sequelae after periods ranging from a few days to 2 weeks. About half the patients were below the age of 10 and almost three-quarters were under 20 years of age.

Specimens of faeces were obtained from 15 patients with typical symptoms and ground with sterile alundum and distilled water, centrifuged at low speed, and the

supernatant fluid treated with ether at 4° C. overnight. The ether was subsequently removed by vacuum. The extracts, proved free from bacteria, were then inoculated intracerebrally and intraperitoneally into 2- or 3-day-old mice. Animals which then showed paralysis or tremors were killed, and pooled suspensions of brain and muscle were passed into a second series of mice. In this way 4 strains of virus were isolated from the 15 specimens, while 5 questionable strains were also obtained. These newly isolated strains were identified as Group-B Coxsackie viruses on the basis of their ability to produce symptoms in very young mice and their inability to infect weaned animals of the same strain. The pathological changes in the tissues of infected animals also corresponded with descriptions given by previous workers.

In order to compare the antigenic relationships among the 4 newly isolated strains of virus, infant mice born of vaccinated mothers were employed. Virgin female mice were given repeated inoculations of live virus. They were then mated and the resultant litters were challenged with the homologous strain of virus, as well as with the other 3 strains. The results showed that the unweaned mice of vaccinated mothers were resistant to several thousand LD50 of each of the 4 strains of Coxsackie virus, while normal control mice became ill in 3 to 4 days and died with typical symptoms. Thus there was a very close if not identical antigenic relationship between the 4 strains of virus.

To demonstrate a relationship between the clinical illness and the virus isolated from stools of patients, neutralization tests were carried out with a constant amount of Coxsackie Group-B virus and varying amounts of serum. Paired serum specimens from typical cases invariably showed a marked rise in neutralizing antibody titre, and single specimens obtained during convalescence showed a significant degree of ability to neutralize the test dose of the virus. *R. B. Lucas*

1417. **Studies on Poliomyelitis in Ontario—V. Further Observations on the Recovery of Coxsackie Viruses from Cases of Clinical Poliomyelitis**
N. Silverthorne, C. Anglin, J. B. J. McKendry, D. S. Knowles, E. M. Clark, F. T. Shimada, A. J. Rhodes, T. E. Roy, R. C. Ritchie, and W. L. Donohue. *Canadian Medical Association Journal* [*Canada med. Ass. J.*] **65**, 536–542, Dec., 1951. 24 refs.

During 1950 the authors examined 22 children admitted to the Hospital for Sick Children, Toronto, suffering from clinical poliomyelitis. Detailed laboratory studies were carried out with a view to differentiating clinically between Coxsackie and poliomyelitis infections and to determining the frequency with which Coxsackie infections simulate poliomyelitis.

The cases in which Coxsackie viruses were isolated from the stools and those in which they were not could not be distinguished on clinical grounds. From the stools of 8 patients, 8 strains of Coxsackie virus were recovered; 6 of these strains produced well-marked myositis in 3-day-old mice, and 2 strains produced lesions in fatty and brain tissue. Tests for homologous antibody were carried out on sera obtained during the acute and convalescent stages from 5 of the patients whose stools contained strains producing myositis in mice. Antibody to the strain of virus isolated from the stool was found in the convalescent phase in 4 of these, and in 2 cases a well-marked rise in antibody titre occurred during convalescence. Homologous antibody was present in the serum during the acute phase in the other 2 patients, but did not increase in the later samples. However, these 2 sera were obtained 9 days after the onset of the illness. One patient excreted Coxsackie virus, but samples of serum collected 11 and 49 days after onset contained no demonstrable antibody. The serological results suggest that 4 of the patients excreting Coxsackie virus had definitely been infected with it; 2 of these patients, who had paralytic symptoms, also excreted poliomyelitis virus; the other 2 patients did not excrete poliomyelitis virus, and appeared clinically to suffer from an attack of non-paralytic poliomyelitis. Exactly one-half of the total number of patients suffered from paralytic poliomyelitis, and poliomyelitis virus was isolated from the stools of all, whereas of the 11 patients with non-paralytic poliomyelitis Coxsackie virus was recovered from the stools of 5, but in no case could poliomyelitis virus be isolated.

The authors conclude that in Toronto in 1950 a substantial number of all patients with poliomyelitis, paralytic or non-paralytic, were excreting Coxsackie virus and that many of those patients diagnosed as suffering from non-paralytic poliomyelitis were probably in fact infected with Coxsackie virus and not with that of poliomyelitis. They suggest that the double excretion of poliomyelitis and Coxsackie viruses probably means only that the two infections have similar epidemiological characteristics. *K. S. Zinnemann*

1418. **Prophylactic Immunization and Poliomyelitis**
J. Lieben. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **83**, 8–13, Jan., 1952. 6 refs.

See also Bacteriology, Abstracts 1206–9.

1419. **Complications after Smallpox Vaccination.** (Verwikkelingen na inenting tegen pokken)
M. A. J. G. H. Smeets and J. M. Soeters. *Maandschrift voor Kindergeneeskunde* [*Maandschr. Kindergeneesk.*] **19**, 325–337, Oct., 1951. 6 figs.

In Breda, Holland, 57,000 subjects were vaccinated within 5 days. In a number of them secondary recurrent vaccinia pustules developed 30 to 32 days after vaccination. There were 4 cases of post-vaccinal encephalitis, all in children of 9 to 11 years of age, in 2 of whom the vaccination was primary. In one of the latter, who had been unsuccessfully vaccinated in infancy, the temperature fell by lysis after the administration of liver extract; the other recovered without treatment. The clinical symptoms in both these cases were similar. The other 2 patients with encephalitis had both been vaccinated in infancy, one without success. Both were treated with corticotrophin, starting with 60 mg. daily and gradually

decreasing the dosage, and temperature became normal within 24 hours.

Clinical details are given and the value of corticotrophin in the treatment of post-vaccinal encephalitis is discussed. *H. Vervoort* [*Excerpta Medica*]

1420. **A Test for the Rapid Diagnosis of Smallpox.** (Eine Schnelldiagnose der pocken)
M. KAISER. *Zeitschrift für Tropenmedizin und Parasitologie* [*Z. Tropenmed. Parasit.*] **3**, 230–233, Oct., 1951. 8 refs.

The author stresses the importance of the rapid recognition of smallpox, particularly from the point of view of a ship's doctor, who is unlikely to have access to laboratory facilities. He recommends the simple test introduced by Tieche 35 years ago, based on the allergic reaction developing in the skin of an immune person within a few hours of inoculation of variolous or vaccinial material. The suspected material is suspended in 2 ml. of 50% glycerin and part is taken up into a capillary tube and heated for 5 minutes in boiling water. Phenolized glycerin is similarly treated and used as control material. Drops of the suspension and control are placed on the skin of the immune person and 2 scarifications made through each, an area of erythema developing around the test scarification indicating a positive reaction. The result can be read in 2 to 4 hours, or frequently earlier if the doctor is accustomed to using himself as the immune person and is consequently aware of the rapidity of his response. Material from varicella vesicles gives no reaction. *D. R. Seaton*

1421. **Clinical Evaluation of Aureomycin and Chloramphenicol in Herpes Zoster**
E. H. KASS, R. R. AYCOCK, and M. FINLAND. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 167–172, Jan. 31, 1952. 25 refs.

An analysis of observations made on 72 patients with herpes zoster reveals no measurable effect of the use of aureomycin or chloramphenicol as compared with the use of a simple analgesic. The lesions cleared within 2 weeks after their first appearance in more than 75% of the patients, and pain was completely relieved in less than 2 weeks from its onset in more than 50%, irrespective of the type of therapy. Post-herpetic neuralgia (pain of more than 1 month's duration) occurred in 13 (18%) of the 72 cases. *J. E. A. O'Connell*

1422. **Investigations of the Preferences shown by *Aedes* (*Stegomyia*) *aegypti* Linn., and *Culex* (*Culex*) *fatigans* Wied., for Specific Types of Breeding Water**
T. MANEFIELD. *Proceedings of the Linnean Society of New South Wales* [*Proc. Linn. Soc. N.S.W.*] **76**, 149–154, Nov., 1951. 11 refs.

Both *Aëdes aegypti* and *Culex fatigans* prefer water containing manure to perfectly clean water. *C. fatigans* refuses to breed in perfectly clean water, and its larvae are more resistant to heavy contamination and to a surface scum of manure than those of *A. aegypti*.
G. M. Findlay

INFECTIVE HEPATITIS

1423. **Incidence of Hepatitis among Narcotic Addicts in the Harlem Hospital**
A. ALTSCHUL, P. D. FOSTER, S. S. PALEY, and L. TURNER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 24–31, Jan., 1952. 15 refs.

The occurrence of hepatitis among drug addicts, who use unsterilized syringes previously used by other addicts, is now well recognized. Five cases of hepatitis are recorded amongst drug addicts in New York, all of whom took heroin (diacetylmorphine hydrochloride) by the intravenous or subcutaneous route. Four patients were definitely jaundiced and one had evidence of hepatitis without evidence of jaundice.
G. M. Findlay

1424. **Epidemic Hepatitis: Prolonged Observation on the Clinical Course with Liver Biopsy Studies**
A. W. BARILE, J. T. TAGUCHI, and S. N. MAIMON. *Gastroenterology* [*Gastroenterology*] **19**, 755–770, Dec., 1951. 6 figs., 23 refs.

The authors studied 25 patients at the U.S. Veterans Administration Hospital, Dayton, Ohio, each of whom "gave an unequivocal history of viral hepatitis", and reached the conclusion that needle biopsy of the liver was the only reliable method of demonstrating and determining the severity of chronic hepatic disease in such patients. They found clinical appraisal of little value, and the liver function tests frequently gave normal results when demonstrable disease was present. [However, when the findings in these tests were abnormal, hepatitis was usually present.]

Active hepatitis was present in 4 patients 1 to 4 years after the initial attack, but in these as in the other cases repeated hepatic biopsy suggested that a steady improvement could be expected with the passage of time. No evidence of cirrhosis was found in any of the 25 patients, even though there had been recurrent jaundice in 10 cases. Among the possible factors complicating the evaluation of these cases the authors stress alcoholism, which was marked in 4 and moderate in 2 of the 10 cases with histological abnormalities in the liver.

[It seems difficult to regard a history of infective hepatitis as "unequivocal", particularly when, as in one patient, the attack of jaundice occurred 28 years previously. This difficulty is emphasized by another of the cases included in the series, which the authors finally diagnosed as of infectious mononucleosis.]
Richard Terry

1425. **The Diagnosis of Hepatitis**
V. M. SBOROV and T. C. KELLER. *Gastroenterology* [*Gastroenterology*] **19**, 424–440, Nov., 1951. 8 figs., 25 refs.

The relative value of the various methods of investigation in the early diagnosis of infective hepatitis was studied by the authors at a U.S. Army hospital for hepatic diseases in a series of 221 patients, of whom 156 had acute viral hepatitis in the first, second, or third

week after the onset of jaundice, 48 had chronic viral hepatitis, and 17 had extrahepatic obstructive jaundice. The clinical information available in each case included the history, the results of physical examination, and the initial results of a varying number of liver function tests. In acute and chronic cases of viral hepatitis diagnosis was confirmed by hepatic biopsy or from the subsequent course of the disease, in the obstructive cases by laparotomy. The tests employed were, in order of frequency: serum bilirubin level (1-minute and total); bromsulphalein retention; thymol turbidity; cephalin–cholesterol flocculation; zinc sulphate turbidity; urine bilirubin and urobilinogen content; thymol flocculation; and serum alkaline-phosphatase and cholinesterase activity.

A prodromal stage was present in 80% of cases of acute viral hepatitis, sometimes with fever lasting 5 to 7 days and with symptoms which might or might not suggest the diagnosis of hepatitis. The liver was seldom enlarged at this stage, but was often tender. Some of the laboratory tests became positive early, particularly the bromsulphalein retention test, the one-minute plasma bilirubin determination, and the urine urobilinogen content. This last was found to be a useful daily routine check.

In the acute stage, lasting 7 to 12 days, the liver was enlarged and very tender, both anteriorly and posteriorly, on palpation or percussion, pain over the liver sometimes persisting for several hours after palpation; the spleen also was sometimes palpable and tender. In some cases, in which all the symptoms were present without clinical jaundice, the use of laboratory methods was especially important. No one liver function test, however, was found to be specific for infective hepatitis, although in many cases a tentative diagnosis could be made from the combined results of the first battery of tests.

There was little difference between the results of the thymol turbidity, cephalin–cholesterol flocculation, and urinary bilirubin tests during the first, second, and third weeks after the appearance of jaundice, the number of positive results increasing with the serum bilirubin level irrespective of the time from the onset. The urinary urobilinogen content decreased as the jaundice increased, the number of cases with urobilinogenuria being at its greatest when the serum bilirubin was less than 5 mg. per 100 ml. When positive, the thymol turbidity, cephalin–cholesterol, and zinc turbidity tests helped to differentiate viral from obstructive jaundice. Needle biopsy of the liver in the acute stage in 46 cases (2 to 45 days after onset of jaundice) revealed a variable but characteristic picture. The lobular pattern was unaltered. There was a diffuse mononuclear infiltration of the lobules, the cells being usually within the sinusoids and in small focal aggregations. The portal canals were " widened " and there were accumulations of monocytes and a few eosinophils in the connective tissue. The Kupffer cells were prominent and contained a granular, yellowish pigment. The nuclei of the parenchymal cells were irregular in size and showed mitotic figures. Hyaline acidophil cells were present. There was no increase in fibrous tissue or bile ducts. The degree of cellular change was not uniform, even in different areas of the same liver at the same time. The lesions in the later cases differed only in degree from those in early cases, and there was little correlation between the clinical severity of the case and the histological findings.

The symptoms of chronic viral hepatitis were sometimes in direct continuation of those of the acute stage, but more often there was an interval of months or years. It is suggested that clinical diagnosis of chronic viral hepatitis is legitimate when signs of hepatic dysfunction persist or recur 6 months or more after the original attack. The clinical picture in the authors' series varied from complete incapacity, with jaundice, to mild symptoms, especially of fatigue. The commonest symptoms were aching in the right upper abdominal quadrant, easy fatigue, and intermittent nausea. The most prominent signs were enlargement of the liver, with tenderness on palpation and percussion, and spider angiomata. The results of serial laboratory tests were not necessarily correlated with the prevailing clinical state. Urobilinogen was commonly present in the urine, and the bromsulphalein and zinc sulphate turbidity tests were usually positive. Jaundice was not a prominent feature, but the serum bilirubin level was sometimes increased.

Liver biopsy was a useful diagnostic help, although the appearances varied widely and there was often no correlation between the clinical findings and histological picture. Scattered focal accumulations of mononuclear cells were seen in the tubules, and collections of similar cells in the portal tracts. There was usually evidence of regeneration of parenchymal cells, such as variation in size of the nuclei, irregular staining, and binucleate forms. Slight or considerable increase in fibrous tissue in the portal tracts and a great increase in bile ducts occurred in some cases. Fatty changes were not constant.

B. G. Maegraith

See also Hygiene and Public Health, Abstract 1220.

BACTERIAL DISEASES

1426. **Leprosy and Sarcoid. The Kveim Test in Leprosy Patients and Contacts**

H. W. WADE. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **17**, 337–347, Dec., 1951. 37 refs.

The author, working in the Culion Leper Colony, Philippine Islands, reports the results of injecting Kveim antigen in 10 cases of leprosy and 7 leprosy contacts. Reviewing the literature, he notes the belief, current during the 1930's, that the aetiology of Boeck's sarcoid was closely related to that of leprosy. It may be impossible to distinguish histologically between the skin lesions of sarcoid and the tuberculoid form of leprosy: there is the same massing of epithelioid cells and giant-cell formation in both. Acid-fast bacilli can be identified in sections from a case of leprosy, but it may take many serial sections to reveal their presence. The lepromin (Mitsuda) reaction, which is positive in almost all cases of tuberculoid leprosy, gives fewer positive readings in sarcoid patients than in the general population. Adenopathy and bone lesions are found in sarcoid, but when they occur in leprosy they are met with not in the tuberculoid, but in the lepromatous type.

The material for the Kveim antigen used by the author was derived from two spleens removed from patients with sarcoid. Antigen from both had proved active when tested on cases of sarcoid. Injection of such material in cases of true Boeck's sarcoid gives rise to long-delayed nodular lesions. The subjects investigated were lepers of the lepromatous type or healthy members of the laboratory staff who were regarded as leprosy contacts. All had been tested with lepromin, providing a full range of reactions from negative to strong positive. The Kveim antigen provoked an early oedematous reaction in all subjects within 24 hours. This subsided within 72 hours in all cases, leaving an induration which did not increase in size thereafter, but subsided slowly. Induration could still be identified in some subjects up to 5 weeks. The significant observation was, however, that it did not progress after the seventh day, and hence the Kveim test could be regarded as negative. The author concludes that there is no aetiological relationship between leprosy and Boeck's sarcoid. *William Hughes*

1427. **Results of Sulphone Therapy of Leprosy in French Guiana.** (Quelques conséquences, en Guyane française, de la sulfonothérapie antilépreuse)
H. FLOCH and G. NOMDEDEU. *Médecine Tropicale* [*Méd. trop.*] **11**, 921–927, Nov.–Dec., 1952. 8 refs.

As a result of intensive treatment with sulphones, discharges from leper hospitals are becoming more and more frequent, a fact which is raising the problem of how to readapt cured lepers for work in the world. The results of treatment depend on the duration of the disease before treatment is begun. Of 584 very advanced cases of leprosy treated at the Sanatorium Padre Bento in French Guiana, only in 8% did the lesions disappear completely, whereas in 158 moderate cases the proportion was 53% and in 99 cases of incipient leprosy it was 66%. Chaulmoogra oil has now been discarded altogether in the treatment of leprosy in French Guiana.
G. M. Findlay

1428. **Sulfoxone Sodium (Diasone) in the Treatment of Leprosy. A Summary Analysis of Field Reports**
E. R. KELLERSBERGER and W. RULE. *International Journal of Leprosy* [*Int. J. Leprosy*] **19**, 265–275, July–Sept., 1951. 3 refs.

In this paper are summarized the results obtained by the medical departments of certain missionary societies throughout the world in the treatment of leprosy. In 21 reports, embracing a total of 661 cases, the data were enough to permit of analysis. The patients were divided into three groups: 187 who had taken diasone for 3 to 6 months; 415 who had taken it for 7 to 12 months; and 59 who had taken it for 13 to 24 months. Of the whole series of 661 patients, 74·8% were clinically improved, 18·8% remained unchanged, and 5·2% became worse; 2·6% died. Surprisingly, the improvement rates appeared to decrease with prolongation of treatment, suggesting in many cases a regression after an initial improvement. This finding, however, was not invariable. Details of results are also given by regions, and show improvement rates varying from 91·4% in Central Africa to 31·8% in China.

Diasone was most effective in clearing the nasal passages and in promoting the healing of ulcers. It was effective to a lesser extent in its action on skin nodules, and least effective on nerve lesions. As regards bacteriological changes conflicting reports were obtained. The incidence of drug reactions—notably headache, anaemia, leucopenia, eczema, and lepra reactions—was 28·4%. There were 17 deaths, at least 3 of them due to the drug. [There is no comparable control group, however.]

The general impression of the investigators as to the efficacy of the drug is favourable, but its potential toxic properties are stressed. *J. L. Markson*

1429. **Double Enteric Infection (*la fièvre typholde intriquée*). An Account of an Epidemic**
A. BATTY SHAW and H. A. F. MACKAY. *Journal of Hygiene* [*J. Hyg., Camb.*] **49**, 299–314, June–Sept., 1951. 2 figs., bibliography.

In April, 1948, just before the evacuation of British troops from Palestine, 76 cases of enteric infection occurred in Acre among soldiers and members of the Palestine Police following a breakdown of chlorination procedure of the contaminated drinking-water supply. *Salmonella typhi* (Vi-phage Type T) and/or *Salm. paratyphi B* (Vi-phage Type Dundee) were found in 74 of the 76 cases, *Salm. typhi* alone in 43, *Salm. paratyphi B* in 3, and both organisms in 28 cases. Three patients died (mortality rate 3·9%), all of them infected with *Salm. typhi* only. Apart from the fatal cases, the severity of the disease was much the same in those infected with *Salm. typhi* alone as in those infected with both organisms. *W. G. Harding*

1430. **Factors Influencing the Results of Blood Culture in Enteric Fever**
A. BATTY SHAW and H. A. F. MACKAY. *Journal of Hygiene* [*J. Hyg., Camb.*] **49**, 315–323, June–Sept., 1951. 43 refs.

The blood-culture results obtained during the outbreak described in the previous paper (see Abstract 1429) are analysed.

Altogether 192 blood cultures were taken and in 71 out of 76 cases a positive result was obtained, despite the fact that all the patients had been inoculated with T.A.B. Positive cultures were obtained from afebrile as well as from febrile patients; at body temperatures between 102° and 104° F. (39° and 40° C.) all cultures were positive. In the whole series the highest percentage of positive cultures was obtained in the second week, but in severe cases the highest number of positive cultures was obtained during the third week. It was found that cultures may have to be incubated well beyond 5 days; 17% of the positive blood cultures required 9 to 11 days' incubation. *W. G. Harding*

1431. **Typhoid Fever; Chloramphenicol Therapy and the Problem of Relapse**
W. V. MATTEUCCI, N. H. SCHIMMEL, and W. P. BOGER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **222**, 446–451, Oct., 1951. 3 figs., 16 refs.

1432. **Typhoid Spondylitis.** (Las espóndilitis tíficas)
M. MARINI. *Cirugía del Aparato Locomotor* [*Cirug. Apar. locomotor*] **9**, 1–22, Jan., 1952. 11 figs., 17 refs.

The author describes 11 cases of vertebral osteitis following typhoid fever, observed at the Istituto Rizzoli at Bologna. In 7 cases the lumbar spine was affected alone, the 3rd lumbar vertebra being the commonest site; in 2 cases the process affected the dorso-lumbar junction; while in the 2 remaining cases the 6th cervical and a dorsal vertebra were respectively involved.

The history, benign course, absence of abscesses, and, radiologically, the early disappearance of the intervertebral space together with comparatively little destruction of the vertebral body clinch the diagnosis. The intervertebral disk appears to be the site of the primary skeletal focus, followed by the spinous or articular processes.

[The radiographs reproduced do not all permit close scrutiny of what are claimed to be typical changes.]
L. Michaelis

1433. **The Treatment of Pertussis with Aureomycin, Chloramphenicol, and Terramycin**
L. WEINSTEIN, R. SELTSER, and C. T. MARROW. *Journal of Pediatrics* [*J. Pediat.*] **39**, 549–559, Nov., 1951. 28 refs.

From a study of the effect of aureomycin, terramycin, and chloramphenicol on 19, 25, and 36 cases respectively of whooping-cough in the Massachusetts Memorial Hospitals, the authors conclude that none of the drugs reduced the incidence of paroxysms. [There is no mention of controls in this part of the study.] The bacteriological data showed that neither aureomycin nor chloramphenicol promptly eradicated *Haemophilus pertussis* from the respiratory tract, but that " terramycin appeared to be the most active in eliminating the infecting agent ". The incidence of complications (12%) was also lowest in the cases treated with terramycin. " In order to evaluate critically the effect of chemotherapy in the incidence of secondary bacterial complications, the records of 139 patients with this disease who received no drugs were studied; about half had received immune serum. . . . The incidence of complications in untreated cases was 10% less than when aureomycin was used and about 4% smaller than when chloramphenicol was given. The only agent which produced fewer complications than were observed in the control group was terramycin." [There has been no attempt to show that the " controls " were at all comparable with the experimental groups other than to note that the age distribution was the same.] *John F. Loutit*

1434. **Control of Pertussis in Day-nursery Contacts with Chloramphenicol**
A. BOGDAN. *Lancet* [*Lancet*] **2**, 1204–1205, Dec. 29, 1951. 3 refs.

At the Westminster Children's Hospital, 11 susceptible contacts of pertussis were given 125 mg. of chloramphenicol 6-hourly for 6 days during the incubation period or early paroxysmal stage; treatment was then changed to a special cholesterol-coated tablet of chloramphenicol containing 100 mg., which was given for a further 6 days. In 2 cases no symptoms developed, in 6 the disease was arrested at the pre-paroxysmal stage, and in 3 it showed no modification. The value of bacteriological examination in making an early diagnosis is stressed, for the results seemed better in those treated at the end of the incubation period or early in the paroxysmal stage. There were no adequate controls.

[The abstracter found it very hard to check the different figures in text and tables owing to the discursive style adopted. This method of treatment may have very important applications, so that it is hoped that the ultimate results of the investigation carried out by this special clinic will be described in more precise detail.]
T. Anderson

1435. **Aureomycin Treatment of Diphtheria and Diphtheria Carriers**
S. KARELITZ, H. KING, and I. S. RUBINSTEIN. *Journal of Pediatrics* [*J. Pediat.*] **39**, 544–548, Nov., 1951. 2 figs., 7 refs.

Aureomycin, in dosage of 25 to 50 mg. per kilo body weight given in 4 equal doses each 24 hours, shortened the carrier period for *Clostridium diphtheriae* in 13 patients with faucial diphtheria and in 5, possibly 6, out of 13 diphtheria carriers. It did not prevent the development of toxic myocarditis in one very sick patient.—[Authors' summary.]

TUBERCULOSIS

1436. **Artificial Pneumothorax. A Survey of a Personal Series**
F. SCADDING, H. NICHOLSON, and C. HOYLE. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **20**, 313–334, Oct., 1951. 14 refs.

The authors describe, from the Brompton Hospital, London, a series of 50 patients in whom artificial pneumothorax (A.P.) was induced on 54 occasions between 1935 and 1944, and who had been observed for a minimum of 5 years and a maximum of 15 years. The patients were under the continuous supervision of one physician, which the authors consider an important factor.

Of the 54 pneumothoraces, 18 were induced for infiltrative disease alone and 36 for infiltration with a cavity which, except in 3 cases was less than 5 cm. in diameter. Adhesions were present in 45 cases, and in 44 cases thoracoscopy was performed, generally within 2 months of the induction of the A.P. In 15 cases atelectasis developed following this, and in addition atelectasis occurred in 7 cases after induction of A.P. The lung became aerated again quickly in all but 4 of these 22 cases, and only 2 of these were troublesome. Pleural effusion occurred in 30 cases, but was not more frequent in patients who had had only a short period of rest before induction of the A.P. In 15 of these fluid did not reach above the diaphragm and had little effect, except in 4 cases where it probably led to obliterative changes and early abandonment of the A.P. In the other 15 cases there were large effusions, 8 of these following division

of adhesions. These effusions occurred more commonly when there were persisting adhesions, and persistent cavitation and active disease in the lung appeared to increase the likelihood of their formation. The chief danger of these effusions was tuberculous empyema, which occurred in 8 of the 15 cases.

The A.P.s were divided into three types: (1) complete and with no pleural adhesions; (2) adequate partial, where adhesions did not seem to interfere with relaxation of the diseased areas; and (3) inadequate partial, where adhesions appeared to be interfering with the relaxation of the diseased area. In the first two groups 17 cavities were present, and all were controlled; in the third group there were 20 cavities, of which 14 were closed, 3 with the aid of a phrenic paralysis.

In 5 cases the A.P. was abandoned before 3 years, and only one of these patients remained well without further treatment. In 7 other cases the A.P. became obliterated after 3 years. In all cases cavities remained closed after expansion of the lung, but 2 patients subsequently died. Of 26 patients whose A.P. was intentionally abandoned after an average period of 5·3 years, 22 are well and at work, 1 died of an intercurrent disease and 1 of pulmonary tuberculosis, and 2 have relapsed. In the remaining 12 patients the A.P. is maintained and is controlling the disease.

Of the 50 patients, 38 are alive and working, 6 have died from tuberculosis and 1 from another disease, and 5 have relapsed. *G. M. Little*

1437. **Atelectasis of the Healthy Lobe in Pneumothorax Therapy**
E. V. Hess. *Tubercle* [*Tubercle, Lond.*] **32**, 237–238 and 254, Nov., 1951. 4 figs., 1 ref.

The author describes 4 cases of atelectasis of a healthy lower lobe occurring in patients with pulmonary tuberculosis treated by artificial pneumothorax at Clare Hall Hospital, South Mimms, Hertfordshire. In 3 of these cases this condition occurred after thoracoscopy, and in 2 of them a subsequent thoracoscopy showed the presence of emphysematous bullae. In one case the atelectatic lobe re-expanded after aspiration of air, but in the remainder continuous suction through an intercostal tube was necessary.

The author tentatively concludes that a reflex mechanism (Xalabarder, *Tubercle, Lond.*, 1949, **30**, 266) is probably of aetiological significance. *R. H. J. Fanthorpe*

1438. **Bronchography in Pulmonary Tuberculosis. With Histopathologic Correlation in 82 Resections**
M. G. Buckles, W. L. Potts, H. B. Davidson, and W. B. Neptune. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **64**, 394–407, Oct., 1951. 6 figs., 8 refs.

From July, 1947, to October, 1949, at the Benjamin Franklin Hospital, Columbus, Ohio, 222 consecutive patients were subjected to bronchography and bronchoscopy, and resection was performed in 82. Iodized oil was used with local anaesthesia in all cases. The only complication noted was atelectasis in one case, successfully treated by bronchoscopic aspiration. The authors differentiate between bronchiectasis distal to tuberculous bronchitis and pure tuberculous bronchiectasis, in which there is tuberculous destruction of the bronchial wall. The results are instructive. Bronchography demonstrated bronchiectasis in 115 of the 222 cases. Of the 82 patients who underwent resection, bronchography showed bronchiectasis in 60, but confirmation was obtained on post-operative examination in only 44. It is suggested that the discrepancy may be due to misreading of bronchograms, especially where bronchi were distorted or crowded, or to confusing oil-filled cavities with dilated bronchi.

Tuberculous bronchitis was seen at bronchoscopy in 9 of the 82 patients subjected to resection, but post-operatively it was found to be present in 35 cases. True tuberculous bronchiectasis was found on section in only 2 cases. *S. F. Stephenson*

1439. **Exudative Pleurisy in Relation to Pulmonary Tuberculosis.** (Forholdet mellem pleuritis exsudativa og lungetuberkulose)
E. Hovesen. *Nordisk Medicin* [*Nord. Med.*] **47**, 118–119, Jan. 25, 1952. 6 refs.

The author studied the relation of exudative pleurisy to pulmonary tuberculosis, using for the purpose the records of the Aarhus Kommune Hospital during the period 1937–46. It was found that in almost all cases exudative pleurisy was either of tuberculous origin or was followed by the development of pulmonary tuberculosis, while 61 (6%) of the 1,015 tuberculous patients admitted between 1937 and 1946 had a history of pleurisy verified by *x* rays or paracentesis. The radiographs of these patients showed pleuritic residues in 47 cases. The tuberculous process was apical in 56 cases (91·8%), mostly on the side of the former pleurisy.

With reference to the frequently discussed question of the period during which a patient who has suffered from exudative pleurisy should be kept under observation, the author emphasizes that only in a little more than half these cases (32) did lung lesions develop within 5 years of the pleuritic attack, and within 10 years in 74% (45). *E. S. Fountain*

1440. **The State of the Cochlear and Vestibular Apparatus in Children with Tuberculous Meningitis.** (Состояние кохлеарного и вестибулярного аппарата у детей при туберкулезном менингите)
Z. S. Benenson. *Вестник Ото-рино-ларингологии* [*Vestn. Oto-rino-laryng.*] No. 4, 29–37, 1951. 5 figs., 13 refs.

Disturbances of cochlear function were noted in 52 out of 76 cases of tuberculous meningitis in 32 boys and 44 girls aged 3 to 16 years. Deafness was complete in both ears in 4 cases, some residual hearing was present in 2, complete unilateral deafness in one, gross hearing loss in both ears in 3, and gross unilateral hearing loss in 6 cases. As the meningitis cleared up, 18 patients showed recovery of hearing loss. Hearing was tested to whisper, speech, and tuning-forks. Streptomycin was administered by the suboccipital route; 5 cases are analysed in detail. In 2 streptomycin toxicity was

considered to be the cause of persistent loss of hearing in view of absent meningitic sequelae. In 3 cases which came to necropsy, and in which the dosage of streptomycin was too small to cause toxic change, destruction of both insulae was found in one case, changes in the 8th nerve nuclei in the second, and involvement of the 8th nerve trunks in granulation tissue in the cerebro-pontine angle in the third.

Loss of labyrinth excitability to caloric stimulation was noted bilaterally in 15 patients, on the right side alone in 8 patients, and on the left side alone in 3 patients. Vegetative reactions were noted in 8 patients, in 6 before streptomycin therapy. Loss of labyrinth excitability was present in 4 patients before treatment with streptomycin began. Among 17 children who had cochlear and vestibular disturbances before streptomycin therapy there were 5 with low-tone deafness. In 3 of these hearing by air conduction was diminished, with lessened bone conduction, and in 2 the lower-tone limit was shortened. In 2 of these children cochlear function recovered. *Stephen Suggit*

1441. **Factors Affecting Prognosis of Tuberculous Meningitis Treated with Streptomycin**
L. FINBERG. *Pediatrics* [*Pediatrics*] **8**, 768–771, Dec., 1951. 6 refs.

Between September, 1946, and November, 1950, 35 cases of tuberculous meningitis (in 32 of which the tubercle bacillus was definitely demonstrated) were treated with streptomycin in the Baltimore City Hospitals. The usual procedure in these cases was to give an intramuscular injection of 50 mg. streptomycin per kg. body weight daily for 90 days, and an intrathecal course of 30 injections, each of 10 to 50 mg. streptomycin, extending over 8 weeks. The total course was repeated if there were signs of relapse. The average course for a survivor was about 100 days. Since 1948 this treatment has been reinforced with various sulphonamides.

Tables are given to show the survival rate of patients under this therapy. The mortality was greatest in the first 18 months of treatment; thereafter relapses were rare. Additional tables are presented to show the serious effect of concomitant miliary tuberculosis with meningitis on the mortality rate, and it is recommended that reports on cases of tuberculous meningitis should always state whether or not miliary tuberculosis is also present. It is further suggested that cases complicated in this way should be described and tabulated separately from cases of uncomplicated tuberculous meningitis.
A. T. MacQueen

1442. **Effect of Combined Therapy (Dihydrostreptomycin and PAS) on the Emergence of Streptomycin-resistant Strains of Tubercle Bacilli**
S. J. SHANE, J. H. LAURIE, C. RILEY, and M. BOUTILIER. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 132–134, Jan. 24, 1952. 12 refs.

At the Point Edward Hospital, Sydney, Nova Scotia, 17 cases of moderately or far advanced pulmonary tuberculosis were treated with dihydrostreptomycin alone in a dose of 1 or 2 g. daily for 90 days, and 32 similar cases with the same dosage of dihydrostreptomycin together with 5 g. PAS daily for a similar time.

The streptomycin sensitivity of organisms in the sputum was determined monthly. In the group treated with dihydrostreptomycin alone, of 11 positive cultures of *Mycobacterium tuberculosis* obtained at the end of treatment and up to 16 months after the start of treatment 2 strains were sensitive and 9 resistant. In the group treated with PAS in addition, out of 21 cases in which positive cultures were obtained 15 strains were sensitive and 6 resistant.

[The proportion of cases developing resistance with this small quantity of PAS is much larger than that reported in the M.R.C. trial, where 20 g. of PAS was given daily and only in 5 out of 48 cases did resistance develop.] *G. M. Little*

1443. **Results of Streptomycin Therapy in Urinary Tuberculosis: a Four Year Review**
R. M. NESBIT and R. L. THIRLBY. *Transactions of the American Association of Genito-urinary Surgeons* [*Trans. Amer. gen.-urin. Surg.*] **43**, 48–52, 1951. 1 fig.

This report is based on a study of 64 cases of urinary tuberculosis treated with streptomycin in the University of Michigan Hospital, Ann Arbor. Antibiotic therapy was used in conjunction with standard methods of treatment, including surgery where applicable and sanatorium care. Patients with no radiological evidence of gross destructive lesion received streptomycin, 1 to 2 g. (or dihydrostreptomycin, 2 g.) daily for 90 days, and were then reviewed. Patients with unilateral destructive lesions received similar treatment for 30 days and, in the absence of improvement, were then subjected to nephrectomy before completion of the course. With severe unilateral renal destruction earlier nephrectomy was performed and the 90-day treatment continued. All cases were reviewed at intervals of 3 to 6 months.

The 44 cases in which a remission occurred have remained free from clinical evidence of tuberculosis from 6 months to 4 years later. Some cases responded to a second course of treatment despite evidence of antibiotic resistance *in vitro*. Of 21 patients with bilateral renal infection (many of whom had had a previous nephrectomy) remission occurred in 12, and of 29 unilateral cases remission occurred in 21; of 14 patients with residual cystitis or genital tuberculosis there was remission in 11. Correlation with the radiological evidence indicated remission in 18 of 25 renal cases without cavitation and 8 of 18 cases with destructive lesions. A table dealing with the relapses shows that most occurred within 6 months of ceasing treatment. [It is not stated how many of the cases were followed up for a longer period than this.] *J. D. Fergusson*

1444. **Tests for Streptomycin Sensitivity of *M. tuberculosis* on Solid Medium**
J. FIELDING. *Tubercle* [*Tubercle, Lond.*] **32**, 210–213, Oct., 1951. 4 refs.

See also Bacteriology, Abstracts 1213 and 1216; Hygiene and Public Health, Abstract 1224.

History of Medicine

1445. **The Study of the Brain and Philosophical Speculation in Ancient Greece.** (Hirnforschung und philosophische Spekulation im griechischen Altertum)
K. SCHLECHTA. *Centaurus* [*Centaurus, Kbh.*] **1**, 334–355, 1951. 14 refs.

Galen, in addition to giving an excellent description of the human brain, made many psychological speculations. His first theory was that the brain pneuma originated chiefly from inspired air which penetrated into the ventricle through the breathing mechanism. Later he believed the life-process to be transformed in the arterial network at the base of the brain into the spiritual soul. If the pneuma flooded into the brain cavities in too great a quantity then the posterior brain cavity, it was believed, stretched like a balloon so that the brain would not be damaged. Although these theories were no longer tenable after Vesalius, credit must be given to Galen for his continual search for some anatomico-physiological relationship—a systematic insistence on a comprehensive " wholeness ". The teaching of Galen, which with that of Hippocrates became dogma to succeeding generations, united the Hippocratic, Hellenic, and contemporary theories of philosophy and natural science. No clear demarcation existed in antiquity between philosophy and science, so there was a constant mixing of pure discovery with " proofs " derived from speculative principles. Galen's physiological, anatomical, and psychological theories were based on a long and extraordinarily involved tradition which in itself was a tangle of empiricism and speculation, only made comprehensible by going back to Aristotle.

Aristotle believed that warmth and pneuma with which man was born were the dominant factors of organic life and that the heart, the fountain of life and of all movement and sensitivity, was the source of warmth and the seat of the physical pneuma. Just as the heart was supposed to radiate warmth, so the brain generated cold to reduce the warmth in the heart. As the cooling apparatus for the blood the brain was regarded as of less importance than the heart. Among his many explanatory theories Aristotle pointed out that the heart had the chief and most noble position in the body, being in the centre; from this he was led to the assertion that the heart must also be the seat of feeling, and the source of nutrition of the soul, of all sense organs, and of those connected with them. One of Aristotle's most important theories was that the power of thought and understanding was not connected with any organ but was above anything of a material nature. Doctors and philosophers, however, must in general have believed in the brain as the dominating life-force. Both Alkmaion, an important authority on this subject, and Plato had regarded the brain as a kind of central depository of the soul, but Aristotle, although conversant with their works, remained unshaken in his beliefs. In his *Timaios* Plato outlined a detailed study of the functions of the human brain, and Alkmaion described the connexion between the brain and the senses such as sight, smell, and taste, distinguishing also between the thinking process and observation.

Between the times of Aristotle and Galen there was much development, of an empirical and speculative nature, in the study of the brain. Two theories had a particular influence—the pneuma and the ventricular—and over these the anatomist, physiologist, and psychologist were engaged in lively controversy. The pneuma principle provided the strongest connexion in the relation between philosophy and medical psychology. It was regarded as the link between soul and body. It was not of one type or form, and its relation to the soul, to warmth, fire, ether, and matter varied and was often scarcely comprehensibly determined. It was of little wonder that later ages found here inexhaustible material for speculation. Up to the time of Galen no important progress was made on the pneuma theory. For him, as for Aristotle, the pneuma was a medium between the spiritual soul and material change to be brought about by it. But the soul according to Galen was seated in the brain.

For almost 2,000 years the doubts and arguments continued as to whether the heart or brain was the seat of the soul, the life-force, the source of warmth and movement. Leonardo da Vinci joined in the speculation, but he wrote in the dawn of a new age, for 24 years after his death Vesalius's great pioneering work was published.

Ruth Hodgkinson

1446. **Dr. Francesco Antommarchi, Anatomist and Napoleon I's Last Physician.** (Chi fu veramente il Dott. Francesco Antommarchi, anatomista e ultimo medico di Napoleone I)
I. CAPPELLINI. *Rivista di Storia delle Scienze Mediche e Naturali* [*Riv. Storia Sci. med. nat.*] **42**, 216–258, July–Dec., 1951. 34 refs.

Francesco Antommarchi, a Corsican by birth but for long resident in Tuscany, occupied an important post in the Hospital of Santa Maria Nuova in Florence, where he had studied anatomy under Paolo Mascagni, and after Mascagni's death in 1815 he was asked to edit Mascagni's anatomical works. At about the same time he became acquainted with Simone Colonna, also a Corsican, who had been in the French administration in Italy, and through Colonna the Bonaparte family requested Antommarchi to become physician to Napoleon, who was then interned on St. Helena. Antommarchi accepted, but his resignation from the staff of the hospital and his departure from Tuscany were actively hindered by the government, since Napoleon's power was still feared. At this time also, John Webb, a merchant well known in Leghorn and a member of the society responsible for the publication of Mascagni's works, wrote

a letter to the British Ambassador at the Court of Tuscany in which he expressed fears that the Corsican physician might take advantage of the liberality of the Prince Regent of England, to whom his *Introduction to the Works of Mascagni* was dedicated, and further that Antommarchi had more talent for intrigue than for medicine. This was the beginning of the campaign which pursued him for the rest of his life.

However, Antommarchi went to St. Helena with the manuscripts of Mascagni and worked on them until he returned to Italy in 1821, after Napoleon's death. The heirs of Mascagni wished to assume responsibility for the publication of the work on anatomy, but Antommarchi, who had devoted so much toil to the anatomical tables, was determined to retain some interest in their disposal, This led to an open quarrel and Antommarchi—who, as Napoleon had noted, was somewhat headstrong—published his *Anatomy*, almost all the illustrations in which were copied from Mascagni, although some of it was his own original work. This plagiarism is, however, excusable as copyright was not so clearly recognized at that time, and the obstinate Antommarchi had resented the underhand methods used to deny him the fruits of his labour.

Later he went to Warsaw, where he was welcomed, then removed to New Orleans, and eventually died from yellow fever in Cuba in 1838. *H. P. Tait*

1447. **Leprosy in Strasbourg.** (La lèpre à Strasbourg) R. BURGUN. *Strasbourg Médicale* [*Strasbourg méd.*] **2**, 723–739, Nov., 1951. 4 figs., 14 refs.

After a few brief notes on the history of leprosy in Europe, especially in the Middle Ages, the author turns to the question as it concerns Strasbourg in particular.

In the Middle Ages the only prophylactic measure was isolation; then came segregation by grouping the afflicted in leprosaria. About 1350 there were 59 such institutions in Paris alone, and 49 along the Rhine. It is said that " collective isolation of lepers " existed at Strasbourg as early as the 10th century. At first they were under the care of the Church, but, later, difficulties arose with the rector of the local church, and in 1309 a lay administration was appointed. The leprosarium was situated to the north of the town, near the Red Church, where now is the Sainte-Hélène Cemetery. It consisted of a house for males and one for females, small dwellings for those wishing to live alone, a summerhouse for the hot weather, and a house for the chaplain.

The author briefly notes later developments. In 1440 a document of 287 articles was drawn up; it inculcated compulsory notification by doctors, " barbers " (surgeons), midwives, and domestics. Any notified patient was seen by two doctors and two " barbers ", and if the diagnosis was confirmed he was separated from his family. Wealthier patients who were not willing to enter the leprosarium had to live in the country, but were obliged to pay one-twentieth of their fortune, or a sum of 40 livres, to the institution. Other rules guided procedure, payments, penalties, and disposal of the belongings of patients. The rules allowed inmates to visit the town, but they were restricted to certain streets, might not go in companies of more than 8, and might not visit the fish-market and other shops, churches, or public baths. They were particularly forbidden to micturate near dwellings or in gardens, for fear of spreading contagion. In fact, it seems to have been a happy organization with as little personal interference as possible compatible with safety. At the same time, those afflicted were regarded as dead to the world, and leprosy was a recognized ground for divorce. [But it should be remembered that in those days the term " leprosy " covered almost any skin disease, infectious or not.]

It is stated that towards the end of the 17th century (1678) there were no more patients arriving, and the decision was reached to demolish the building. (It was actually closed some years later.) It is estimated that the number of lepers never exceeded 1 per 1,000 of the population [but the value of such an estimation is doubtful, as diagnosis was far from certain, some lepers lived outside the town, and probably many cases were hidden].

Nothing is said regarding treatment at the institution, but the author refers to a medical work of the 15th or 16th century which has several chapters on the disease—its names and synonyms, its causes (quartan and intermittent fever among them), and symptoms. Treatment is also dealt with in this publication. Between 1519 and 1526 a work was published by Strasbourg physicians pointing out the distinctions between itch, cancer, fistula, and leprosy; according to them the last was caused by " bad and corrupted [*empoisonné*] air, insanitary dwellings, noxious trees around dwellings, fever, excessive eating, and stimulating beverages ". Johann Winter von Andernach (1487–1574) published a medical work in Basle in which he stated that leprosy may be inherited, but that it has a long latent period and affects adults only, the young and adolescent being immune. [He does not attempt to harmonize this with the fact that the disease may be hereditary.] It may be conveyed by contact or appear spontaneously. In 1673 Benjamin Niesius chose leprosy as the subject for his inaugural thesis. He recognized infection by contact, by miasma, by bedclothes, by feeding utensils, and by corpses. The disease may also, he says, be acquired congenitally; it may skip a generation, and men are more often affected than women. In 1685, when the leprosarium at Strasbourg was about to be demolished, Sebiz and Mappus, in a work reviewing skin diseases, pointed out the differences between " lepra Graecorum or psoriasis and lepra Arabum ", the latter being " very repulsive, highly contagious, and incurable ". They were in advance of many medical men of their day in maintaining that among the so-called lepers were patients suffering from harmless skin diseases. *H. Harold Scott*

1448. **Smallpox and Variolation: their Historical Significance in the American Colonies**
S. S. BERNSTEIN. *Journal of the Mount Sinai Hospital, New York* [*J. Mt Sinai Hosp.*] **18**, 228–244, Nov.–Dec., 1951. 7 figs., 16 refs.

Variolation, which was practised widely throughout the Orient as early as the 6th century A.D., was introduced into Western Europe by way of Constantinople and

became an accepted method of immunization in England at the beginning of the 18th century. In the American colonies at that time epidemiological control measures were of the crudest nature. Smallpox cases were removed to the local pest-house, but quarantine laws were totally inadequate. When Boston was visited by an epidemic for the sixth time in 1721, the case mortality was nearly 1 in 7 and few families escaped the infection. A few days after the appearance of this epidemic Cotton Mather, a famous fundamentalist divine, circularized the physicians of Boston urging them to inoculate the inhabitants with the contents of smallpox pustules, a practice of which the physicians were entirely ignorant, but which had been described to Mather by slaves as customary among African tribes. Mather's campaign met with a storm of abuse, but despite the outcry one Boston physician, Zabdiel Boylston, was persuaded to inoculate. Boylston issued a progress report after 6 months showing the salutary effect of inoculation, and very slowly the opposition began to abate and inoculation was finally accepted. At the invitation of Sir Hans Sloane, President of the Royal College of Physicians, Boylston came to London in 1724 and during his stay of 2 years lectured to the College on several occasions. He was elected a Fellow in 1726 and in the same year published a treatise on inoculation in New England. From Boston the practice of variolation gradually spread throughout the colonies and the technique was steadily improved. Although in 1753, when Boston was again visited by a smallpox epidemic, 1 in 10 of the uninoculated died, compared with only 1 in 68 of the inoculated, the practice fell into disrepute in several areas because of the number of untrained and unscrupulous people who became " inoculators ", and certain provinces, such as Virginia, New Hampshire, New York, and Connecticut, expressly forbade inoculation.

With the outbreak of the War of Independence in 1775 the most dangerous enemy of the colonists was smallpox. Washington battled heroically against the threat of the disease amongst his troops, and many of his movements were determined by the fear of smallpox. In June, 1776, half the 10,000 men of the Northern army were unfit for battle, chiefly as a result of its ravages. The British, on the other hand, protected partly by a natural immunity gained in their overcrowded towns and partly by the established practice of inoculation, suffered hardly at all from the disease. Washington eventually succeeded in inducing Congress to legalize inoculation for the entire army in January, 1777, and within a few weeks the disease was almost completely eradicated. This also removed the chief obstacle to recruitment and, with its increased strength, the colonial army ultimately forced the English to surrender in 1781. *Ruth Hodgkinson*

1449. **Thomas Addison and the Background to Cortisone**
F. G. YOUNG. *British Medical Journal* [*Brit. med. J.*] **2**, 1535–1541, Dec. 29, 1951. 25 refs.

In this paper is described the " enormous oak which has grown from the acorn that Addison unobtrusively planted in Guy's Hospital in 1855 ". Addison's monograph *On the Constitutional and Local Effects of Disease of the Supra-renal Capsules* is discussed, and it is noted that of the 11 cases described by him only 4 can be confidently accepted as being true cases of his disease. When Addison wrote, the nervous system was normally thought to be the sole coordinating mechanism of the body. Hormones were far in the future. Yet Addison seems to have had the germ of an idea that non-nervous coordinating mechanisms might exist, as indeed had Richard Lower 200 years earlier. The views of de Bordeu, George Gulliver, A. A. Berthold, and Claude Bernard are also noted, and special attention is given to Pavy's criticisms of Bernard's work.

From this point the development of endocrinology is reviewed through the work of Brown-Séquard, Hilton Fagge, Ord, Oliver and Schäfer, and many others until the outstanding contribution to adrenal research of Swingle and Pfiffner is reached. The physiology and biochemistry of steroids in general, and cortisone in particular, are then discussed in some detail, and stress is laid on the theory that cortisone does not act directly on a toxin or noxious stimulus, but is effective in conferring on a cell the ability " to withstand abnormality in the internal environment ". *Calvin P. B. Wells*

1450. **An Historical Account of Enuresis**
L. B. GLICKLICH. *Pediatrics* [*Pediatrics*] **8**, 859–876, Dec., 1951. Bibliography.

The need for the medical treatment of enuresis has been recognized ever since the writing of the Ebers papyrus of 1550 B.C. Although ethnographers have paid scant attention to the subject, enough has been written to show that even in a primitive civilization treatment presents a problem. In the West African kingdom of Dahomey, for instance, if training and a beating have not corrected the habit by the age of 4 or 5, ashes and water are poured over the child's head and he is driven into the streets, where for his benefit the children sing " Adida ga ga ga ga " (urine everywhere). Little attention was devoted to the subject until the 18th century, treatment varying from supplication to patron saints such as St. Vitus and St. Catherine to the taking of concoctions of which ground testicle and hedgehogs were frequent ingredients. Thomas Phaer's *Boke of Children* devotes only a paragraph to the subject under the title " Of Pyssying in the Bedde ".

The 18th century found the anatomical idea influencing medical treatment to an increasing extent, and effectiveness was claimed for the application of blisters to the sacrum, this being suggested by the fact that the afferent nerves of the bladder pass through the foramina of the sacrum. With the advent of the 19th century the growing interest in sanitation gave impetus to the study of enuresis, which came to be regarded as a social and economic hazard: the child of the rich was made ineligible for school, while few households would employ a maid who wet her bed. The spate of theories and treatments reached their zenith about the middle of the century. Too deep sleep, imbalance of the vesical musculature, irritation of the urinary tract, desire perpetuated by habit, broken neurogenic communication between inhibitory centres in the brain and the spinal cord, and

many other theories were suggested. All the drugs in the pharmacopoeia were advocated in treatment, but the most widely used were strychnine with a view to improving the tone of the sphincter, belladonna, chloral hydrate, and cantharides. General measures, such as adjusting diet, limiting fluid intake, and awaking the child just before the time at which he usually wet the bed, were also adopted. Numerous manipulations and gadgets were designed, especially for the unfortunate male child. Various penile bandages, collodion poured into the prepuce, and bungs were doubtless effective therapy, but among the doctors who disagreed with their use was one who had seen two cases in which the penis had been cut through.

Enuresis in the present century has been considered in terms of personality disorder and psychology. The concept of conditioning the child has led to the invention of a number of ingenious gadgets; one such releases a stream of cold water as soon as the child micturates.

Ruth Hodgkinson

1451. **Sir William Gowers at the National Hospital**
G. HOLMES. *British Medical Journal* [*Brit. med. J.*] **2**, 1397–1399, Dec. 8, 1951.

1452. **John Quincy, M.D. (*d.* 1722), Apothecary and Iatrophysical Writer. A Study of his Works, including his Commentary on Santorio, his *Compleat English Dispensatory*, and his *Lexicon Physico-medicum***
N. HOWARD-JONES. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **6**, 149–175, 1951. 3 figs., 3 refs.

1453. **Erasmus and his Diseases**
H. N. COLE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 529–531, Feb. 16, 1952. 12 refs.

1454. **An Early Prepayment Plan for Medical Care. The Thomsonian System of Botanical Medicine**
W. G. SMILLIE. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **6**, 253–257, 1951.

1455. **Nathaniel Wallich, Surgeon and Botanist (1786–1854)**
J. SEIDE. *Medicine Illustrated* [*Med. ill.*] **6**, 91–92, Feb., 1952. 1 fig.

1456. **The Life and Times of William Gosse**
C. O. F. RIEGER. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 281–284, Sept. 1, 1951.

1457. **Josef Breuer: the Great Viennese General Practitioner**
B. JUHN. *Medicine Illustrated* [*Med. ill.*] **6**, 33–34, Jan., 1952.

1458. **Philippe Pinel (1745–1826). His Views on Human Nature and Disease. His Medical Thought**
W. RIESE. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **114**, 313–323, Oct., 1951. 9 refs.

1459. **Henry Bence-Jones, F.R.S., 1813–1873**
L. H. SAVIN. *King's College Hospital Gazette* [*King's Coll. Hosp. Gaz.*] **30**, 132–134, 1951.

1460. **John Machin, Mathematician and Astronomer, and the First Description of Ichthyosis Hystrix**
W. R. BETT. *British Journal of Dermatology* [*Brit. J. Derm.*] **64**, 59–60, Feb., 1952.

1461. **Tomás Romay and the Yellow Fever**
J. LÓPEZ SÁNCHEZ. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **6**, 195–208, 1951. 2 figs., 7 refs.

1462. **Walter Reed. "He Gave to Man Control of that Dreadful Scourge—Yellow Fever"**
W. B. BEAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 171–187, Feb., 1952.

1463. **The Self-education of Young John Hunter**
F. BEEKMAN. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **6**, 506–515, 1951. 14 refs.

1464. **Contemporary Portraits of Ambroise Paré. With Particular Reference to the Painting in Possession of the New York Historical Society**
J. DOE. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **7**, 1–9, 1952. 11 figs., 10 refs.

1465. **Dr. Halsted**
G. J. HEUER. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **90**, Suppl., 1–105, Feb., 1952. 15 figs.

1466. **Sir William Macewen**
A. R. JONES. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **34-B**, 123–128, Feb., 1952. 1 fig., 11 refs.

1467. **Charles Clay: the Father of Ovariotomy in England**
W. F. SHAW. *Journal of Obstetrics and Gynaecology of the British Empire* [*J. Obstet. Gynaec. Brit. Emp.*] **58**, 930–940, Dec., 1951.

1468. **Woodward and the Changing Concept of Cancer, 1858–1873**
H. W. EDMONDS. *Military Surgeon* [*Milit. Surg.*] **109**, 314–321, Oct., 1951. Bibliography.

1469. **Obstetrics in Ancient India**
K. B. RAO. *Journal of the Indian Medical Association* [*J. Indian med. Ass.*] **21**, 210–213, Feb., 1952. 9 refs.

1470. **New Contributions to the Iconography of Paracelsus.** (Neue Beitrage zur Ikonographie von Paracelsus)
J. STREBEL. *Gesnerus* [*Gesnerus*] **8**, 236–245, Feb., 1952. 1 fig.

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